ACCULTURATION, BODY MASS INDEX AND TYPE 2 DIABETES RISK IN ASIAN AMERICANS

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ABSTRACT

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(Under the direction of June Stevens)

Exposure and assimilation to a Western environment (acculturation) might impact the health of Asian immigrants to the US. This hypothesis is supported by the lower prevalence of overweight and diabetes in Asians living in Asia compared to those living in the US, but longitudinal studies are lacking. We conducted a longitudinal analysis on 8,634 Asians using data on acculturation (generational status, length of US residence, age at immigration) and BMI history from the California Men's Health Study (2002-2003) and information on repeated, measured BMI and diabetes diagnoses from electronic health records (2005-2012). We determined: (1) differences in BMI changes in Asians living in Asia versus Asians living in the US; (2) the association between acculturation, overweight and BMI change after immigration to the US; and (3) BMI's role as a mediator of the association between acculturation and incident diabetes.

We confirmed that Asians living in Asia experienced smaller increases in BMI over time than those living in the US at the same age. After immigration to the US, first-generation, foreign-born Asians gained weight rapidly during their first 25 years in the US, yet they never reached the same level of overweight as their second- and third-generation, US-born counterparts. Contrary to our expectations, Asians born in Asia had a higher risk of diabetes than those born in the US despite their lower BMI levels. Thus, Asians might be exposed to risk factors, other than BMI, prior to migrating to the US. Less acculturated Asians were at even

higher diabetes risk when we considered the effect independent of BMI using mediation analysis. Their lower BMI levels protect less acculturated Asian men from diabetes.

These results provide novel insights into the influence of a Western environment on BMI and diabetes risk among Asian immigrants and emphasize the importance of public health efforts in this vulnerable ethnic group, which already has elevated diabetes risk at the time of immigration. Interventions focused on maintaining a healthy weight are needed for Asians immediately after immigration to the US.

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LIST OF ABBREVIATIONS

BMI	Body mass index
CHD	Coronary heart disease
CMHS	California Men’s Health Study
CVD	Cardiovascular disease
IP	Inverse-probability
IRB	Institutional review board
KG	Kilogram
M	Meter
MSM	Marginal Structural Model
NHLBI	National Heart, Lung and Blood Institute
NIH	National Institutes of Health
SD	Standard deviation
UNC	University of North Carolina
US	The United States of America

I. INTRODUCTION

A. Background

The number of Asian immigrants to the United States (US; Asian Americans) grew six times faster than the general US population in the 1990's[1]. Asians recently surpassed Hispanics as the largest group of new immigrants to the US, and in 2010, 430,000 Asians moved to the US whereas new Hispanic immigrants numbered 390,000[2]. Nevertheless, there are comparatively few studies on the chronic disease risk of Asian Americans, and the paucity of longitudinal work is especially striking. This surprisingly thin literature is made more troubling by findings that Asians living in the US have a higher prevalence of overweight and obesity compared to Asians living in their ancestral countries[3,4], and they may be at greater risk of diabetes at a lower body mass index (BMI) compared to other ethnic groups because they have more body fat (and less muscle) and more abdominal fat at the same BMI level[5-8]. The obesogenic environment in the US fuels high levels of CVD-related risk in Americans including highly susceptible Asian immigrant populations assimilating to American norms. Thus, it is possible that Asian immigrants to the US are threatened by a double burden as high levels of risk associated with Asians living in Asian countries are compounded by exposure to an obesogenic environment that fuels high levels of CVD-related risk in America.

Studying disease rates in genetically similar immigrant populations who undergo drastic environmental and lifestyle changes allows us to determine the health effects of changing environmental exposures. Specifically, this dissertation research provides insight into the complex interrelationship between acculturation and adiposity with diabetes risk in Asians living in the US and has the potential to inform policy as well as medical and public health practice relevant to this important and growing American ethnic group. Acculturation is defined for our purpose as a cultural change from a traditional Asian lifestyle to a Western lifestyle when migrating from Asia to the US. We used epidemiologic tools and examined extant data from the California Men's Health Study initiated by Kaiser Permanente of Northern and Southern California. We emphasized longitudinal approaches to avoid biases inherent in studying these issues in cross-sections. In addition, we studied Asians with different countries/regions of origin combined and separately to determine possible differences among Asian subgroups. Specifically, we examined men of Chinese, Japanese, Korean, Filipino and Vietnamese descent who immigrated to, or grew up in the US.

B. Research Aims

The aims of this research were as follows.

Aim 1. Determine the association between US residence compared to residence in an Asian country and changes in BMI with aging.

Aim 2. Determine the association between acculturation and overweight (BMI ≥25 kg/m^2) as well as BMI change during US residence. Acculturation was defined in terms of generational status, length of US residence and age at immigration.

Aim 3. Determine the total effect of acculturation on incident type 2 diabetes as well as the controlled direct effect (independent of BMI) of acculturation on incident type 2 diabetes in Asian American men.

II. LITERATURE REVIEW

A. Asian Americans

1. *Overview*

The National Institutes of Health (NIH) has urged researchers to conduct more studies of cardiovascular disease (CVD) risk among Asian American populations, which are growing rapidly and among whom the burden of CVD is increasing dramatically[9]. Thus, CVD among Asian Americans will be a significant cost burden for the US healthcare system. However, current data on CVD and its risk factors are scarce in this population. Asian Americans are especially susceptible to diabetes, an important CVD risk factor, and have been shown to have double the risk of diabetes than Caucasians[10].

The number of Asian immigrants grew six times faster than the general US population in the 1990s[1]. In 2000, 12 million Asians lived in the US[11] and this number increased to 15 million in 2006[12] with Chinese being the largest subgroup[9]. Asians are expected to comprise 10% of the US population by the year 2050[13,14]. However, Asian Americans are an understudied ethnic group in relation to CVD and most research on acculturation focuses on Mexican Americans, although Asians surpassed Hispanics as the largest group of new immigrants to the US in 2010 (430,000 Asians vs. 390,000 Hispanics)[2].

There have been instances of more personalized treatments in other American ethnic groups[15,16], but not among Asian Americans because of limited studies identifying important risk factors. Results from this dissertation work will be critical in the development of optimal diabetes prevention plans as well as personalized treatment strategies for Asian American minority populations in the US.

2. *Differences in characteristics by Asian subgroups*

Asian Americans are a heterogeneous group of individuals from various countries of origin who differ in important characteristics. Vietnamese living in the US have lower levels of education than other Asian subroups[9] and more than 75% of Japanese and Filipino have incomes that are higher than US average[17]. Asian Americans have lower smoking rates compared to Whites, Blacks and Hispanics, but within Asian subgroups smoking rates are highest among Koreans (22%) and lowest among Chinese (7%). Most Asian Americans are in the normal BMI range, with rates ranging from 51% in Filipinos to 68% in Chinese. Prevalence of obesity is low in the Asian population, but 14% of Filipinos are obese compared to 5% of Vietnamese or 4% of Chinese. Only 3 in 10 Asian adults engage in regular leisure-time physical activity and Vietnamese are most likely to be inactive in their leisure-time (46%). These disparate risk profiles between Asians and other ethnic groups and within the different Asian subgroups themselves[18] indicate the importance of research on subpopulations to adequately assess predictors of elevated BMI and diabetes risk in Asian Americans.

3. *Overweight and obesity in Asians*

In the last two decades prevalence of overweight and obesity has increased sharply in Asian countries[19] and these increases may be linked to Westernization (i.e. adoption of Western culture)[20]. Between 1992 and 2002 China, for example, experienced a 50% increase in overweight and obesity prevalence (1992: 14.6%; 2002: 21.8%)[21]. Despite rapidly increasing BMI levels in Asia, age-adjusted prevalence of overweight ($\geq$25 kg/m^2) is still much lower in adults in Asia compared to adults in the US. The prevalence of overweight and obesity was 69% in the US in 2008[22], while in Asia prevalence was, for example, 25% in the Philippines and 30% in Japan[23]. Estimates of overweight prevalence in Asian Americans from NHANES are not considered reliable because of small numbers[24], but data from the 2010 National Health Interview Survey suggests that Asians living in the US have higher levels of BMI compared to their counterparts living in Asia with an age-adjusted prevalence of 41%[4]. Thus, living in the US might have detrimental effects on the health of Asian immigrants. *Nevertheless, there have been no longitudinal studies of the impact of American acculturation on body weight in Asian immigrants.*

4. *Diabetes burden in Asians*

Prevalence of diabetes increased in some Asian countries, but remained somewhat stable or even decreased in others over the last three decades (e.g. Japan: 3.5% in 1980 and 6.0% in 2008; Philippines: 7.7% in 1980 and 6.6% in 2008)[25]. In the US, however, diabetes is a substantial health burden among Asian Americans. Despite being a well-known CVD risk factor, diabetes alone is also the fifth leading cause of death among Asian Americans with an age-adjusted death rate of 15.5 per 100,000 in 2010[26]. Asian Americans have a higher age-adjusted diabetes prevalence than Caucasians (8.2% vs. 6.0%)[27] and suffer double the risk for type 2 diabetes than their Caucasian counterparts[10].

The limited literature on Asian Americans suggests a large variation of diabetes risk across Asian American subgroups (Chinese, Filipino, Japanese, Vietnamese and Korean). Data from the 2004-2006 National Health Interview Surveys suggest that self-reported diabetes rates are highest among Filipinos and lowest among Koreans (9% and 4%, respectively)[9].

Given that type 2 diabetes is a well-established CVD risk factor with a high prevalence among Asian Americans, it is eminent to determine risk factors specific to Asian Americans that put them at an increased risk of type 2 diabetes. Previous research had difficulty in distinguishing genetic from environmental influences on diabetes. Studying Asian American immigrants allowed us to identify environmental risk factors while holding genetic influences constant[28,29]. An especially important and relevant environmental risk factor for Asian Americans is a cultural change from a traditional Asian to a Western lifestyle when migrating from Asia to the US. Thus, it is crucial to elucidate potential pathways through which acculturation can affect disease risk among Asian American immigrants.

B. Acculturation

1. *Definition*

In the context of this research acculturation is defined as a cultural change from a traditional Asian to a Western lifestyle when migrating from Asia to the US. Only a few small studies have examined how acculturation may impact disease risk in Asian American adults, but acculturation has been hypothesized to exacerbate health problems among Asian Americans. Although CVD rates are drastically increasing in some Asian countries, such as China, the prevalence of CVD in China is still only approximately one quarter of that among Caucasians in the West[30]. Compared to US residents in general, Chinese living in China and Japanese living in Japan have lower CVD rates[31-34] and associated conditions, such as hypertension, hypercholesterolemia, and diabetes[34-36]. Evidence suggests that immigrants have better health compared to native-born individuals ("healthy immigrant effect"), potentially due to the fact that immigrants are positively selected and are hence in better health to withstand the difficult process of migration[37-42]. However, after immigration this health advantage seems to decrease with increasing time spent in the Western country[31,39]. Longer duration of residency in a Western country has been shown to increase CVD risk profiles[43] and to increase risk of coronary calcification among Asians[44]. There is a vast body of literature on the effects of acculturation on Hispanic immigrant population, but studies on Asian immigrants to Western countries are scarce. It has been shown that diverse immigrant groups experience different acculturation processes and, thus, more research on Asian immigrants are essential[40,45].

Differences in levels of acculturation between immigrants can result in different health behaviors, such as dietary habits or physical activity levels, and disease outcomes, such as overweight and obesity[46]. More recent immigrants have lower obesity prevalence than those who have been in the US for longer periods[39,47-49]. This suggests that BMI and subsequent risk for chronic disease increases with increasing length of US residence as discussed below. The underlying assumption is that the obesogenic environment in the US, characterized by inexpensive and abundantly available foods and growing portion sizes as well as increased sedentary behavior[50], favors weight gain and chronic disease among immigrants. This type of environment is thought to be a major driver of the obesity and chronic disease epidemic. Acculturation measures, such as place of birth, length of US residence and age at immigration, can capture the degree of an immigrant's exposure to this obesogenic environment[51].

The pioneer among studies on acculturation in Asians was the Ni-Hon-San Study more than 30 years ago that compared Japanese living in Japan, Hawaii and San Francisco[28]. The authors found that a higher level of acculturation, which was measured using three scales (culture of upbringing, current cultural assimilation and current social assimilation) was related to higher levels of cholesterol, greater prevalence of coronary heart disease, and higher incidence and mortality resulting from coronary heart disease[52-55]. However, this study assessed the effects of acculturation in the 1970s, prior to the nutrition transition in Asia and the obesity epidemic in the US[56,57].

2. *Acculturation and body mass index*

The Honolulu Heart Program was part of the Ni-Hon-San Study and more than 50 years ago recruited 8,006 men of Japanese ancestry living in Hawaii[58,59]. The authors found that a higher level of maintenance of Japanese culture, measured using three self-report scales (culture of upbringing, current cultural assimilation and current social assimilation), was related to lower levels of BMI in a cross-sectional analysis. The mean BMI was 26 kg/m^2 in the lowest quartile of maintenance of Japanese culture and 23 kg/m^2 in the highest quartile ($p<0.05$). This study also examined BMI and prevalence of diabetes (reviewed below) in Asian Americans in relation to proxies of acculturation. Contrary to expectation, the authors found that Japanese who were born in Hawaii did not have a significantly different mean BMI compared to those born in Japan. This may have been because data were collected prior to, or at very early stages of the US obesity epidemic that was first detected in the late 70's, and prior to huge transitions in the economy, lifestyles and obesity prevalence in many Asian countries. Therefore this early research has limited application to recent waves of Asian immigrants to the US.

In some more recent studies of Western acculturation in Asians only crude, unadjusted estimates were shown[60-64] or data from Asians were combined with data from Pacific Islanders[47]. Asians and Pacific Islanders are very different in average adult body mass index[3] and body composition[65] and, therefore, results can be erroneous when they are combined. Putting aside the studies with those flaws, we know of four cross-sectional studies in Asians that have examined differences in BMI by indicators of acculturation and found no association[46,51,66], while six other cross-sectional studies showed a positive association in Asians in both the US and Canada[66-71]. Some of the differences in the literature might be explained by the finding that acculturation seems to affect Asian subgroups differently[72]. Data from the 1997-2005 National Health Interview Survey among 1,651 Central Asians and 2,139 Southeast Asians showed that prevalence of overweight and obesity (BMI ≥25 kg/m^2) increased with length of US residence in Central Asians, but not in Southeast Asians[69]. There are many potential reasons for this observed difference including that these groups experience very different environments and levels of Westernization in their home countries[57,73]. These results emphasize the importance of examining Asians in country or region-specific subgroups.

3. *Acculturation and type 2 diabetes*

We know of only one longitudinal study on diabetes. That study used data on Chinese from the Multiethnic Study of Atherosclerosis and found only 2 cases of diabetes among US-born and 43 cases among foreign-born Asians over a median follow-up time of 5 years. No significant differences were detected, perhaps because of low statistical power.

The Honolulu Heart Program had a larger sample size (n=8,006 Japanese men) but used a cross-sectional design. To our knowledge this ground-breaking work remains the only study to find an association between acculturation and diabetes. The authors concluded that Japanese who were born in Hawaii had a significantly higher age-adjusted prevalence of diabetes compared to those who were born in Japan (63.6 versus 52.4)[58]. This finding remained significant even after adjustment for demographics, BMI, physical activity and diet. However, as previously mentioned, this study used data from a cohort recruited half a century ago and may not be applicable to current waves of Asian immigrants to the US and the current US cultural climate.

4. *Body mass index assimilation as a contributing factor in Asian immigrants changing health*

The specific factors changing Asians' health after immigration are unknown and it is essential to identify how acculturation affects changes in disease risk. It is especially important to identify potential modifiable factors that might mediate the pathway between acculturation and diabetes to identify targets for diabetes prevention strategies among Asian American minority populations. It is logical to hypothesize that changes in BMI at least partially mediate associations between acculturation and disease risk in Asian Americans, but this possibility has been inadequately studied so far[39]. Understanding the obesity and diabetes patterns among immigrant populations is essential since increasing chronic disease rates worldwide and increasing rates of migration can alter chronic disease patterns within and between sending and receiving countries[67].

One longitudinal[74] and two cross-sectional studies[58,61] compared models on the association between acculturation and diabetes without adjustment for current BMI to models with adjustment for BMI. However, this change in estimate approach to study mediation has several assumptions (including no confounding between mediator and outcome) that are difficult to meet[75-77]. In this dissertation we used more robust methods to assess mediation, specifically marginal structural models, and we studied both BMI change and disease incidence longitudinally.

III. METHODS

A. California Men's Health Study (CMHS)

1. *Overview of dataset*

The majority of the general US foreign-born population resides in California and California also houses the largest share of Asian populations (~4.2 million)[13]. Thus, data from California include larger representative samples of Asian immigrants than national surveys and they provide an opportunity to identify potential future obesity patterns across the US[67].

The California Men's Health Survey was initiated in 2002 by Kaiser Permanente of Northern and Southern California, a large, prepaid health plan in California, primarily to study prostate cancer etiology, but secondarily to study non-cancer conditions[78]. Eligible participants were 44 to 71 year old men (mean age: 58.7, SD: 6.8) who were members of Kaiser Permanente. In total 4,010 Chinese, 2,356 Filipino, 1,294 Japanese, 650 Vietnamese and 319 Korean men completed the baseline survey in 2002/03. The baseline survey included questions on demographics, place of birth for the participant and both parents, time lived in the US, education, medical history, prescription and non-prescription drugs and lifestyle. A follow-up survey in 2006 included questions on weight at different ages throughout adulthood and history of diabetes. We merged the CMHS data with the participants' Electronic Health Records from 2005-2012 to get information on disease diagnoses and lab results as well as repeated, clinically measured anthropometrics.

Unfortunately this dataset only includes men; however, data on large samples of Asian immigrants are extremely scarce and, thus, this data still provided a great source to study the effects of acculturation on obesity and chronic disease among Asian immigrants and this dissertation is an essential contribution to determining the causes and prevention strategies of cardiometabolic disease in a new and diverse immigrant population in the U.S. In addition, men tend to be more negatively affected by acculturation than women as they are more likely to be in the workforce, which is associated with increased exposure to the host culture[79].

2. *Variables*

This section describes the assessment of the main variables used in this dissertation work.

a. Ethnicity

Participants reported their race/ethnicity on a screening survey prior to the baseline survey. This information was used to create unique racial/ethnic categories for the following: Chinese, Japanese, Korean, Vietnamese and Filipino. Participants who reported being Mexican, Central or South American, or any other Hispanic are defined as Latino regardless of other race or ethnicity reported and were removed from all other race/ethnic categories to avoid interference of Latino culture with Asian culture in our analyses. The Chinese population included people who were mixed races of Chinese and other races, while the categories of those reporting being Japanese, Korean, Vietnamese and Filipino were mutually exclusive. When sample size allowed Asian subgroups were analyzed separately. Due to small sample size in some analyses we had to collapse the Asian subgroups either into all Asians combined or into a category of “other East Asians” (Japanese and Koreans) and into a category of “Southeast Asians” (Vietnamese and Filipinos). These categories were chosen since East Asians and Southeast Asians have been shown to have similar CVD risk[80], but also based on the similar economic status of their country of origin (GDP per capita in Japan: 33,632; South Korea: 24,801; Vietnam: 2,600; and Philippines: 3,406)[81]. Van Hook *et al.* showed that the effect of acculturation on health differs by the level of economic development in an immigrant's country of origin with those migrating from a country with low GDP being more affected by acculturation experienced in the US than those who migrated from a country with higher GDP[73].

b. <u>Acculturation</u>

Indicators of acculturation included generational status, length of US residence and age at immigration. Participants reported their place of birth as well as their mothers' and fathers' place of birth in the baseline questionnaire in 2002/03. Participants chose from a list of countries and could also specify other countries if their place of birth was not listed. This information was used to categorize men as first-generation (foreign-born participant with foreign-born parents), second-generation (US-born participant with at least one foreign-born parent) and third-generation (US-born participant with US-born parents).

Duration of residence in the US was determined by the question "How many years have you lived in the United States" and participants chose from the categories "my whole life or more than 25 years", "16-25 years", "11-15 years", "6-10 years" and "5 years or less". In our analyses we collapsed these categories into <10, 11-25 and >25 years to provide adequate sample sizes within categories in the smaller groups studied.

We calculated age at immigration by subtracting duration of US residence from age at baseline. Since duration of US residence was collected in ranges as a categorical variable, we determined the age period during which participants immigrated by subtracting the lower and upper bound of the US residence categories from age at baseline. Participants were categorized into ≤40 and >40 years at immigration if both the lowest and highest possible age at immigration fell into the same category. We performed sensitivity analyses to compare use of the extreme high and low values.

c. Self-reported body mass index

Participants reported their weight and height at baseline in 2002/03 and recalled their weight at ages 30, 40, 50 and 60 in the 2006 follow-up questionnaire. BMI (kg/m^2) was calculated at baseline and these four age decades [BMI = (weight in pounds/squared height in inches) x 703] and analyzed as continuous variables.

d. Clinically measured body mass index

Measured weight and height from the Electronic Health Records (2005-2012) was used to calculate BMI (kg/m^2) at each clinic visit. We used an algorithm developed by Dr. Matthew Maciejewski (Durham VA Medical Affairs and Duke University, NC) and Lynne Van Scoyoc (Durham VA Medical Affairs, NC) to clean the weight data. Height was not measured at all clinic visits and, on average, participants had 15 height measurements. To calculate BMI for each year of follow-up we used each participant's average height from his first 15 clinic visits and average weight from each clinic visit within a year. Follow-up and the beginning of each year of observation started with a participant's first weight measurement. The use of average annual weight avoids spurious influences from minor weight fluctuations. Each participant could have up to 8 BMI measurements.

BMI was modeled as both a continuous variable and in categories formed using the current NIH BMI cutpoints (normal weight: 18.5-24.9 kg/m^2, overweight: 25.0-29.9 kg/m^2 and obesity: ≥30 kg/m^2) since the use of Asian-specific BMI cutpoints is controversial[82-85]. However, we performed sensitivity analyses using the Asian-specific BMI cutpoints (underweight: <18.5, normal weight: 18.5-22.9, overweight: 23.0-24.9, obesity I: 25.0-29.9 and obesity II: ≥30.0 kg/m^2)[86]. We also calculated BMI changes between clinic visits and scaled them to 5-year changes.

e. <u>Diabetes</u>

To identify diabetes cases we extracted data on membership, primary care utilization, laboratory tests and pharmaceutical use from health plan electronic databases from 2005-2012. Type 2 diabetes diagnoses are based on four automated health-plan data sources including pharmacy prescriptions for diabetes medications or supplies (insulin, sulfonylurea drugs, metformin, and blood glucose testing supplies), abnormal HbA1c values (>6.7%) in regional laboratory files, primary or secondary hospital discharge diagnosis of diabetes, and emergency department visits for which a physician diagnosis of diabetes was listed[87]. Recommendations for screening tests are not weight related and time intervals for the screening tests are based on the health plans' clinical practice guidelines.

f. <u>Age</u>

Age at baseline, at clinical weight measurements and at diabetes diagnosis was calculated from date of birth and date of baseline survey completion, date of clinic visits and date of diabetes diagnosis, respectively.

g. Education

Participants reported their level of education in the baseline survey by selecting one of the following categories: high school or less, vocational/some college, college graduate or graduate degree.

h. Income

Participants reported their level of income at baseline as <$40,000, $40,000-59,999, $60,000-79,999 and ≥$80,000.

B. Analytic methods

Methods used in the individual studies are summarized in those chapters. Additional methodological details are discussed here.

1. *Generalized estimating equation model*

In Chapter 4 we used generalized estimating equation (GEE) models to estimate the effect of place of residence (US vs. Asia), age at immigration and year of immigration on BMI changes prior and after immigration. GEE models account for the correlation between repeated measures per person[88,89]. We used an autoregressive order 1 covariance structure as it is reasonable for intervals with the same length.

To determine the difference in BMI changes over time in Asians living in Asia versus Asians living in the US we regressed continuous BMI on categorical age at reported BMI (30, 40, 50 and 60 years), country of residence (binary) and an interaction between age and country of residence.

$E(BMI)_{ij} = \beta_0 + \beta_1 \cdot (\text{age at reported } BMI_{ij}) + \beta_2 \cdot (\text{US residence}_{ij}) + \beta_3 \cdot (\text{age at reported } BMI_{ij} \text{ x US residence}_{ij}) + \beta_4 \cdot (\text{covariates})$, where $j=1 \ldots m_i$ and m_i indicates the number of time points for subject i and $i=1 \ldots n$ with n being the total number of subjects. The interaction between age at reported BMI and US residence allowed us to calculate the change in BMI associated with a 10 year increase in age among Asians who live in the US compared to Asians who live in Asia (i.e. the estimated effect of US residence on the age-BMI association).

To determine the difference in BMI change by age at immigration we also regressed continuous BMI on categorical age at reported BMI (30, 40, 50 and 60 years), categories of age at immigration (immigration between ages 19-30, 30-40, 40-50 and 50-60 as well as after age 60) and an interaction between age at reported BMI and age at immigration.

$E(BMI)_{ij} = \beta_0 + \beta_1 \cdot (\text{age at reported } BMI_{ij}) + \beta_2 \cdot (\text{age at immigration}_{ij}) + \beta_3 \cdot (\text{age at reported } BMI_{ij} \text{ x age at immigration}_{ij}) + \beta_4 \cdot (\text{covariates})$, where $j=1 \ldots m_i$ and m_i indicates the number of time points for subject i and $i=1 \ldots n$ with n being the total number of subjects. The interaction term allowed us to estimate the change in BMI associated with a 10 year increase in age comparing Asians who immigrated earlier in life to those who immigrated later in life. This analysis allowed us to determine the effect of age at immigration on BMI changes after immigration to the US and the potential for detecting acculturation effects. We repeated this analysis by replacing age at immigration with calendar years at immigration to determine a potential effect of secular trend on BMI change among Asian immigrant men to the US.

In Chapter 5 we used generalized estimating equation models with an autoregressive order 1 covariance structure to calculate odds ratios (OR) and 95% confidence intervals (CI) of being overweight comparing different levels of acculturation.

$logit[E(Overweight)_{ij}] = \beta_0 + \beta_1 \cdot (measure\ of\ acculturation_{ij}) + \beta_2 \cdot (covariates_{ij})$, where $j=1 \ldots m_i$ and m_i indicates the number of time points for subject i and $i=1 \ldots n$ with n being the total number of subjects. We estimated separate models for each measure of acculturation (generational status, length of US residence and age at immigration).

2. ***Hierarchical linear model***

In Chapter 5 we used a 2-level hierarchical linear model for BMI curves[90] with an autoregressive order 1 covariance structure to determine the association between acculturation and BMI changes in Asians living in the US, using repeated, clinically measured BMI.

- <u>Level 1</u>:

  $(BMI)_{ij} = \beta_{0i} + \beta_{1i} \cdot (age\ at\ BMI\ measurement)_{ij} + \varepsilon_{ij}$, where $j=1 \ldots m_i$ and m_i indicates the number of time points for subject i; $i=1 \ldots n$ with n being the total number of subjects.

- <u>Level 2</u>:

  $\beta_{0i} = \gamma_{00} + \gamma_{01} \cdot (measure\ of\ acculturation)_i + \gamma_{02} \cdot (baseline\ covariates)_i + \delta_{0i}$

  $\beta_{1i} = \gamma_{10} + \gamma_{11} \cdot (measure\ of\ acculturation)_i + \gamma_{12} \cdot (baseline\ covariates)_i + \delta_{1i}$

The error terms (δ_{0i} and δ_{1i}) followed a normal distribution with a mean of 0. Separate models for each measure of acculturation (generational status, length of US residence and age at immigration) were determined.

3. *Cox proportional hazards regression model*

In Chapter 6 the total effect of acculturation on incident diabetes was determined using Cox proportional hazard regression models with age as the time scale to determine the hazard ratio (HR) and 95% confidence interval (CI) of diabetes across different levels of acculturation.

$$\lambda_a(t) = \lambda_0(t)exp^{(\beta_1 a)}$$

where

$\lambda_0(t)$… unspecified baseline hazard

β_1 … log hazard ratio of acculturation

Confounders were controlled for by inverse-probability weighting using the weights described in w_2 in the section below.

4. *Marginal structural models*

In Chapter 6 we estimated the direct effect of acculturation, independent of BMI, on risk of diabetes using inverse-probability (IP) weighted marginal structural models (MSM)[91]. MSM are used to estimate the marginal expectation or distribution of a counterfactual outcome[92]. Our analysis focused on the controlled direct effect, which has the interpretation of the effect of the exposure on the outcome, holding the mediator to a particular level, as if one intervened on it[76,91]. These models assume counterfactual consistency (well defined exposures and mediators), positivity (each subject has the possibility of experiencing each exposure level) and exchangeability (no confounding between the exposure and the outcome as well as no confounding between the mediator and the outcome)[91,93]. The controlled direct effect is preferred in this setting since there may be confounders of the BMI-diabetes association that are effects of the exposure, which precludes identification of natural direct and indirect effects.

In this study, the controlled direct effect describes the effect of acculturation on diabetes independent of BMI (Figure 3.1.). We estimate the controlled direct effect by the method outlined by VanderWeele[91]. The weights for the IP weighted MSM are based on BMI (*M*) conditional on acculturation (*A*) and confounders of the BMI-diabetes relationship (*C*) . The first set of (stabilized) weights, which blocks the pathway from acculturation to BMI (thereby isolating the direct effect of acculturation), and controls for BMI-diabetes confounders, are given by:

$$w_{1,i} = P(M_i = m_i | A_i = a_i) / P(M_i = m_i | A_i = a_i, C_i = c_i).$$

The denominator represents the probability of participant *i* (*i*=1, …, n) having their observed level of BMI given their exposure level (acculturation, *A*) takes the value *a* and the confounder(s) (*C*) take the value(s) *c*. The numerator is the probability of each participant's specific BMI (*M*) conditional on acculturation (*A*) for each individual and is included to improve stability of the final model.

The second set of weights, which controls for confounders of the acculturation-diabetes relationship, are based on acculturation (A) and confounders (C):

$$w_{2,i} = P(A_i = a_i) / P(A_i = a_i | C_i = c_i).$$

The denominator represents the probability of a participant's specific level of acculturation given that the confounder(s) (*C*) take the value(s) c_i while the numerator represents the marginal probability of acculturation (A) for each individual. Each individual's final weight was then calculated as

$$w_i = w_{1,i} \times w_{2,i}.$$

Since exposure and mediator are multilevel categorical variables, multinomial logistic regression models for acculturation and BMI were fit and used to estimate the probabilities in the respective weights. We specified the confounders *C* as, age at baseline, income and education. The final IP weighted Cox MSM was fit using weights as above and terms for the main effects of acculturation (*A*), BMI (*M*) and the acculturation-BMI interaction. We additionally estimated the direct effects of acculturation pooled across levels of BMI, which assumes homogeneity of the effect of acculturation with respect to BMI. The marginal structural Cox model for the controlled direct effect, including the interaction term, is then given by:

$$\lambda_{a,m}(t) = \lambda_0(t)exp^{(\beta_1 a+\beta_2 m+\beta_3 a*m)}$$

where

$\lambda_0(t)$… unspecified baseline hazard

β_1 … log hazard ratio of acculturation

β_2 … log hazard ratio of BMI

β_3 … log hazard ratio of the cross-product of acculturation and BMI

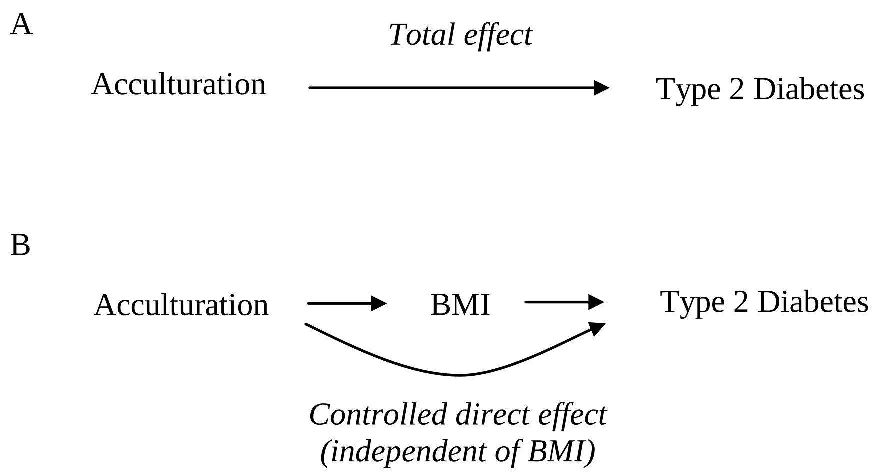

Figure 3.1. The total effect of acculturation on type 2 diabetes (A). Controlled direct effect of acculturation on type 2 diabetes independent of BMI (B).

IV. LONGITUDINAL STUDY OF BODY MASS INDEX IN ASIAN MEN WHO IMMIGRATE TO THE US

A. Abstract

Background: Cross-sectional studies indicate that adaptation to Western norms, especially at a younger age, might explain the higher average body mass index (BMI) among Asians living in the US compared to Asians living in Asia. However, migrants differ from non-migrants in sociocultural factors that are difficult to measure and, thus, longitudinal studies on the same individuals prior to and after immigration are needed.

Objective: To determine differences in changes in BMI across age by residence (US or Asia) and age at immigration using longitudinal data on BMI prior to and after immigration among Asians.

Methods: Data from the baseline survey (2002-2003) and a follow-up survey (2006) of the California Men's Health Study was used. The cohort included 1,549 foreign-born Asian men who were aged 44-71. BMI at ages 30, 40, 50 and 60 was calculated using self-reported weight history and current height. Country of residence at each age decade and age at immigration were estimated. Data were analyzed using generalized estimating equations.

Results: Ten-year BMI increases were smaller among Asians who still lived in Asia prior to migrating to the US compared to those who already lived in the US. This effect was most evident between ages 30-40 when Asians in Asia had a 0.69kg/m^2 (95% CI:-1.08,-0.30) smaller increase in BMI. Immigrants who moved to the US before age 40 experienced greater increases in BMI than immigrants who moved to the US at an older age.

Conclusion: This study is the first to support the hypothesis that living in the US and younger age at immigration results in larger BMI increases in Asian men. Interventions focused on maintaining a healthy weight immediately after immigration should be considered for Asian immigrants.

B. Background

The Asian population in the US (here: Asian Americans) is rapidly expanding with 15 million Asian Americans currently living in the US[12]. Asian Americans in general as well as key subpopulations represent understudied ethnic groups in relation to disease risk[9]. Most research on immigration and acculturation (i.e. transition from a traditional to a Western lifestyle) focuses on Hispanics[94], although new Asian immigrants to the US outnumbered new Hispanic immigrants in 2010 (430,000 vs. 390,000)[2] and the literature on Hispanics cannot be applied to Asians diverse immigrant groups experience different acculturation processes[40,45]. In addition, previous research on Asian Americans combines all Asians into one group and ignores heterogeneity[9,69].

Asian Americans have, on average, a higher body mass index (BMI) compared to Asians living in their ancestral countries[4,95]. This difference may be due to exposure to a Western environment in the US. Extant literature is limited to small, cross-sectional studies and does not fully explore critical aspects of the migration experience. The lack of longitudinal studies is especially troubling because immigrants to Western countries differ from their native counterparts who do not migrate in many environmental and cultural factors that are difficult to measure[37,38]. For example, immigrants in general are healthier and wealthier than their native counterparts who do not migrate, but this health advantage tends to diminish with increasing time spent in a Western country[96]. Previous, cross-sectional studies among Asians in Asia versus Asians in the US were not able to control for these differences in the types of people who choose to immigrate versus those who do not[4,95]. Thus, the role of immigration to the US on the higher levels of BMI observed among Asians living in the US remains uncertain. To answer this question, data on the same individuals before and after immigration are required.

Once immigrants move to the US, they are exposed to a Western obesogenic environment, which is characterized by increased access to energy dense, palatable foods and lifestyles conducive to physical inactivity. This obesogenic environment has been suggested as cause for the excess increase in BMI in Asian immigrants to the US[50]. However, Westernization might also contribute to the increasing BMI levels within Asian countries that were observed in the last three decades[50]. The rates of increasing BMI levels vary across countries[19,51,72]. Men living in Japan, for example, had an age-adjusted mean BMI of 22.1 kg/m^2 in 1980, which increased to 23.5 kg/m^2 in 2008, while among men living in the Philippines BMI increased from 21.2 kg/m^2 in 1980 to 22.9 kg/m^2 in 2008[95]. Although the mean BMI levels remain in the normal range, the overweight prevalence ($\geq$25 kg/m^2) increased from 16.8% and 11.1% in 1980 to 30.1% and 24.5% in 2008 among Japanese and Filipino men, respectively[23]. These trends in immigrants' home countries can influence BMI patterns observed after immigration to the US. It is likely that recent immigrants and those from more developed countries arrive in the US with higher BMI levels that are more similar to levels observed in the US. Thus, exposure to the US environment might be less influential among these immigrants[51,73]. To confirm these assumptions and to control for these differential exposures, studies examining the association between immigration to the US and BMI need to carefully examine their results by Asian subgroups and by year of immigration. Additionally, age at immigration contributes to the degree of an immigrant's exposure to the obesogenic Western environment. Younger age at immigration has been shown to increase later overweight and obesity risk[46,97].

The goal of this study was to determine if changes in BMI across age differ among Asian men who already immigrated to the US compared to those still residing in their country of origin at the same age prior to their migration to the US. Additionally, differences in these changes by age at immigration and year at immigration were determined to examine potential secular trends. The focus of this study was on BMI between the ages 30 and 60 in three Asian subgroups (Chinese, Southeast Asians and Other East Asians). To our knowledge this is the first longitudinal study to examine the effect of moving to the US on BMI changes among Asians.

C. Methods

1. *Study population*

Kaiser Permanente Northern and Southern California health plans initiated the California Men's Health Study in 2002-2003[78]. Eligible participants were 44-71 years old men who had been Kaiser Permanente members for at least one year. The baseline questionnaire collected information on demographics, health status and lifestyle behaviors and was completed by 8,634 men of Chinese, Filipino, Japanese, Vietnamese or Korean ancestry. The following participants were excluded: Asians who were US-born or had missing information on place of birth (n=2,531), those who had lived in the US for >25 years or had missing information on length of US residence (n=3,199) since age at immigration could not be calculated for these participants, those with missing information on weight history (n=1,317), outliers (outside mean±3SD) for recalled weight (n=6) and those who had missing information on height (n=6) or covariates (n=26). The final dataset included 757 Chinese, 18 Japanese, 51 Korean, 519 Filipino and 204

Vietnamese. Vietnamese and Filipinos were combined into a category of "Southeast Asians" (n=723) and Japanese and Koreans into a category of "Other East Asians" (n=69) to increase statistical power. These subgroups were chosen because the groups included in each category have similar cardiovascular disease risk[80] and their countries of origin have similar economic status (GDP per capita in Japan: $33 632, South Korea: $24 801; Vietnam: $2 600, Philippines: $3 406)[73,81]. Chinese were examined as a separate category. This study was approved by the Institutional Review Boards of Kaiser Permanente Northern and Southern California and this secondary analysis was approved by Kaiser Permanente and University of North Carolina at Chapel Hill Non-Biomedical Institutional Review Boards on research involving human subjects.

2. *Measures*

Participants recalled their weight at ages 30, 40, 50 and 60 in a follow-up questionnaire in 2006 and BMI at these four age decades was calculated using height reported at the baseline questionnaire in 2002-03. BMI was analyzed as a continuous variable. The correlation coefficients between clinically measured weight at age 50 (n=91) and at age 60 (n=318) from participants' Kaiser Permanente electronic health records compared to recalled weight at these ages at baseline were 0.95 and 0.93, respectively. The correlation coefficient between clinically measured height and self-reported height at baseline was 0.87.

Years of US residence was assessed in the baseline questionnaire and was used to calculate age at immigration (age at baseline minus length of US residence), which was categorized into 19-30, >30-40, >40-50, >50-60 and >60-68. Year at immigration (date of baseline completion minus length of US residence) was categorized into immigration between 1977-1986, 1987-1991, 1992-1996 and 1997-2003. Participants were assigned to residence in

Asia or the US at each recalled weight based on their age at immigration. Specific time points, not entire participants, for which country of residence was uncertain were excluded to avoid misclassification. In sensitivity analyses observations with missing country of residence were first assigned to living in Asia and then to living in the US. This did not change the conclusions and, thus, excluding these observations did not seem to have biased the results.

3. *Statistical analyses*

Differences in mean BMI at each age decade and differences in BMI changes between age decades by country of residence, age at immigration and year at immigration were determined. The estimates and the associated 95% CI were calculated using generalized estimating equation models with an autoregressive order 1 covariance structure to account for the correlation between repeated BMI measures[88,89]. We regressed continuous BMI on categorical age (30, 40, 50 and 60 years), country of residence (binary) and an interaction between age and country of residence. Including this interaction allowed us to calculate the difference in the change in BMI for participants residing in their country of origin compared to those residing in the US during each specific age decade (i.e. the estimated effect of US residence on the age-BMI association). We also regressed continuous BMI on categorical age (30, 40, 50 and 60 years), categories of age at immigration (19-30, 30-40, 40-50, 50-60 and >60 years) and an interaction between age at reported BMI and age at immigration. This analysis allowed us to determine the effect of age at immigration on BMI changes after immigration to the US and the potential for detecting acculturation effects. Finally, we repeated this analysis by replacing age at immigration with calendar years at immigration (1977-1986, 1987-1991, 1992-1997 and after 1997) to determine a potential effect of secular trend on BMI change.

Estimates were determined for all Asians combined and by Asian subgroups (Chinese, Southeast Asians and Other East Asians). All models were adjusted for age at baseline, annual household income (<\$40,000, \$40,000-59,999, \$60,000-79,999 or ≥80,000) and education (high school or less, vocational/some college, college graduate or graduate degree), which were reported in the baseline questionnaire. The analyses were performed using SAS Statistical Software, version 9.3 (Cary, NC). All tests and p-values were two-sided and considered statistically significant at α=0.05.

D. Results

Participants were on average 56 years old at baseline (Table 4.1). Approximately 30% of Chinese were in the lowest and in the highest income categories. In contrast, most Southeast Asians (55.1%) and Other East Asians (66.6%) had at least a college degree but 55.1% and 52.2% reported <\$60,000 annual household income, respectively. Overweight prevalence (≥25.0 kg/m^2) was heterogeneous between the Asian subgroups (Table 4.1). Among all Asians combined, the overweight prevalence ranged from 9.3% at age 30 when participants lived in Asia to 42.0% at age 50 when participants lived in the US. When living in Asia, Other East Asians had the highest overweight prevalence at ages 30 and 40 and Southeast Asians had the highest prevalence at age 50. When living in the US, Southeast Asians had the highest overweight prevalence at all age decades, except at age 30 where Chinese had the largest proportion of overweight individuals.

BMI increased with age irrespective of country of residence (Figure 4.1). For all Asian men combined, the adjusted mean BMI at age 30 was significantly higher for those who lived in Asia compared to those who lived in the US, while mean BMI at ages 40, 50 and 60 was significantly lower for those who lived in Asia compared to those who lived in the US at the respective age. Similar results were found for Southeast Asians. For Chinese and Other East Asians none of the comparisons were statistically significant.

Comparing BMI changes between age decades by country of residence (Table 4.2) showed that BMI increases over time were less for those who still resided in Asia than those who had immigrated to the US. Yet only the difference in BMI change between ages 30-40 achieved statistical significance with those living in Asia having a 0.69 kg/m^2 (95% CI: -1.08, -0.30) smaller increase in BMI compared to Asians who already immigrated to the US during this time period. A similar trend was observed in each Asian subgroup. For Chinese and Other East Asians none of these comparisons were statistically significant. Among Southeast Asians, differences in BMI changes between ages 30-40 were particularly striking (Asia-US: -1.20 kg/m^2; 95% CI: -1.81, -0.59).

Examining age-related BMI levels by age at immigration showed that Asians who immigrated at an earlier age tended to have larger BMI levels than those who immigrated at a later age (Figure 4.2). Among all Asians combined, participants who immigrated to the US between ages 19-30 or 30-40 had a higher adjusted mean BMI at ages 40 and 50 years compared to other groups. Interestingly, among participants who immigrated between ages 40-50 the mean BMI was lower at ages 40 and 50 compared to those who immigrated earlier, but at age 60 (once they lived in the US) the mean BMI assumed a similar value as participants who immigrated earlier. A similar trend was observed among Chinese. Those who immigrated between ages 19-30 had a higher mean BMI compared to other groups at ages 40 and 50. Finally, among Southeast Asians those who immigrated between ages 30-40 had a higher mean BMI than other groups at age 50. Results for Other East Asians are not shown due to small sample size.

Comparing slopes of BMI across groups of immigrants who moved to the US at different ages (Table 4.3) showed that participants who immigrated at a younger age had a significantly greater increase in BMI over time until age 50 compared to those who immigrated at older ages. Additionally, the increase in BMI between ages 30-40 and 40-50 years was lower among Asians who immigrated after these time intervals compared to those who immigrated before the respective interval, indicating a potential acculturation effect. Similar patterns were observed among the Asian subgroups, but findings were more pronounced among Southeast Asians.

The analyses of year at immigration did not indicate an effect of secular trend on BMI change among Asian immigrant men to the US (Table 4.4). Compared to Asian men who immigrated between 1997-2003, those who immigrated prior to 1997 had similar BMI changes between age decades. The results were consistent across Asian subgroups.

E. Discussion

This study was uniquely able to compare BMI levels and BMI changes associated with exposure to a Western environment and confirmed the hypothesis that the BMI of Asians will increase upon migration to the US. Asian men living in Asia prior to immigrating to the US experienced smaller increases in BMI over time than those who already lived in the US. Asian men who immigrated prior to age 40 were particularly susceptible to larger increases in BMI than Asian men who immigrated later in life. These results demonstrate that early and middle-adulthood might be a vulnerable time period for excess increases in BMI among Asian immigrant men to the US.

To our knowledge, only one previous cross-sectional study has examined the association between age at immigration and BMI among Asian immigrants to the US[69]. This study combined

Central Asians into one category (Chinese, Japanese, Mongolian, North and South Korean) and compared the odds of being overweight among Central Asian immigrants to European immigrants to the US within each category of age at immigration (<18, 18-24, 25-44 and 45-74 years). Within each category of age at immigration Central Asians had lower odds of overweight compared to Europeans. This study did not provide any insight if different ages at immigration might have differential effects on BMI among Asians. Additionally, the authors examined each participant's BMI at only one time point (after immigration to the US) and did not have data on participants' BMI prior to immigration. Two previous cross-sectional studies among immigrants to the US from all continents combined showed that younger age at immigration increased likelihood of being overweight[46,97]. These studies found that those <20 years or <22 years at immigration, respectively, had higher odds compared to those arriving at older ages. This suggests that environmental exposures during childhood or adolescence have substantial influence on adult BMI. The present study adds to this conclusion that immigration during early and mid-adulthood (ages 19-40) may also substantially influence BMI changes later in life, at least in Asian men. In contrast, the hypothesis that exposure to the US environment might be less influential among recent immigrants[51,73] was not confirmed in this study.

In the present study generally similar results were found among the Asian subgroups examined, however, the results were more pronounced among Southeast Asians than the other groups, suggesting that this group might be particularly susceptible to excess increases in BMI after immigration to the US than Asians from other subgroups. This is consistent with the hypothesis of Van Hook and Balistreri who speculated that the effect of exposure to a Western environment on health may differ by the level of economic development of an immigrant's country of origin, with those migrating from countries with low GDP (such as Vietnam or the Philippines) being more affected by acculturation experienced in the US[73].

Changes in diet and physical activity after immigration to the US are likely responsible for the observed excess increases in BMI among Asian immigrants. After immigration to the US Asians consume more sweets and fast foods and fruits, but less meat, meat alternatives and vegetables than when living in their home countries[98]. In addition, levels of physical activity tend to decrease upon migration to the West[99]. It is a limitation of the present study that changes in diet and physical activity associated with immigration could not be determined.

Another limitation is that height was self-reported and weight earlier in life was recalled. Compared to men in other race/ethnic groups, Asian males living in the US have been shown to overestimate their height less and to underestimate their weight more[100]. Nevertheless, self-reported weight does provide a reasonable proxy of measured weight with correlation coefficients above 0.9 for concurrent estimates in East Asian populations[101-103] and in Southeast Asian developing countries where weight is not routinely measured[104]. A study in an American cohort showed that recall of weight much earlier in life (28 years prior) is also highly correlated (r=0.82) with weight measured at that time[105]. These relatively high correlations between clinically measured weight and recalled weight at ages 50 and 60 (r>0.9) as well as clinically measured and self-reported height at baseline (r=0.87) suggest that the self-reported height and recalled weight used in the present study are adequate. The Asians included in this present study might not be generalizable to all Asian immigrants to the US since they were members of Kaiser Permanente, had health insurance and lived in a region (California) with a large Asian population. Compared to the 2000 census, our sample was slightly more educated (20% vs. 15% with less than a high school degree) and had a slightly higher income (37% vs. 22% with annual household income of <$40,000)[106]. Additionally, given the strict exclusion criteria to answer this research question, the final dataset included only 18% of all Asian men in the California Men's Health Study. Given the small sample size we were not able to perform a comprehensive analysis of a potential age-period-cohort effect, but we examined age at immigration as well as year at immigration to determine potential age and secular effects. Despite these limitations, this study provided the unique opportunity to examine the effects of immigration on BMI change among Asian men.

Strengths of this study included the comparably large sample size of Asian Americans, an understudied population. Additionally, Chinese, Southeast Asians and Other East Asians were examined separately to determine differential effects of acculturation by region of origin, and the same individuals were examined across different migration stages (pre- and post-migration) to reduce the potential for bias from healthy immigrant selection as discussed earlier. This bias potentially undermines estimates that solely compare the average BMI in Asian countries to the average BMI among Asians in the US[4,95]. Additionally, the effects of year at immigration on BMI were examined to rule out potential bias of the age at immigration analyses by secular trends.

Recent analyses of the National Health and Nutrition Examination Survey showed that despite a much lower prevalence of overweight ($\geq$25 kg/m^2) among Asian adults (38.6%) compared to Caucasian adults (66.7%) and Hispanic adults (78.8%), Asians had a similar prevalence of hypertension as the other two ethnic groups (approximately 25%)[107-109]. Asians may be at greater risk of diabetes and cardiovascular disease at a lower BMI compared to Caucasian populations because they have more body fat and more abdominal fat at the same BMI level[5,6,8,110]. Our finding that Asian immigrants experience larger increases in BMI after immigration to the US is, therefore, troubling as these increases in BMI could lead to dramatic increases in chronic diseases in this minority population. Medical and public health practice for disease prevention need to focus on maintaining a healthy weight among Asian immigrant men.

Table 4.1. Characteristics of study sample, California Men's Health Study

Characteristics	All Asians (n=1,549)	Chinese (n=757)	Southeast Asians (n=723)	Other East Asians (n=69)
Age at baseline in years [mean (SD)]	56.4 (6.9)	56.3 (7.2)	56.5 (6.5)	56.6 (7.2)
Education [%]				
≤ High school	21.6	27.9	15.2	20.3
Vocational/some college	27.1	25.9	29.7	13.0
College graduate	33.7	23.9	43.2	42.0
Graduate degree	17.6	22.3	11.9	24.6
Annual household income [%]				
<$40,000	29.7	29.6	30.2	26.1
$40,000-59,999	23.6	22.1	24.9	26.1
$60,000-79,999	17.3	15.5	18.8	21.7
≥$80,000	29.4	32.9	26.1	26.1
Proportion overweight (≥25 kg/m^2) [% (n of all participants in particular category)]				
In Asia (prior to immigration to the US)				
At age 30	9.3 (n=787)	5.7 (n=436)	12.4 (n=323)	28.6 (n=28)
At age 40	19.4 (n=417)	14.0 (n=215)	23.7 (n=190)	50.0 (n=12)
At age 50	24.4 (n=86)	17.3 (n=52)	35.5 (n=31)	33.3 (n=3)
At age 60	0 (n=6)	0 (n=5)	0 (n=1)	-- (n=0)
In the US (after immigration)				
At age 30	16.7 (n=54)	19.2 (n=26)	16.7 (n=24)	0 (n=4)
At age 40	32.4 (n=641)	24.2 (n=310)	41.4 (n=297)	29.4 (n=34)
At age 50	42.0 (n=1,126)	34.3 (n=569)	50.9 (n=507)	40.0 (n=50)
At age 60	40.7 (n=727)	32.2 (n=366)	49.7 (n=332)	44.8 (n=29)

Table 4.2. Differences (95% CI) in BMI change among Asian men living in Asia compared to those living in the US[a]

	BMI change between ages 30 & 40		BMI change between ages 40 & 50		BMI change between ages 50 & 60	
	Estimate (Asia-US)	**95% CI**	**Estimate (Asia-US)**	**95% CI**	**Estimate (Asia-US)**	**95% CI**
All Asians	**-0.69**	**-1.08, -0.30**	-0.10	-0.39, 0.19	-0.43	-0.94, 0.09
Chinese	-0.31	-0.84, 0.21	-0.04	-0.41, 0.33	-0.38	-0.98, 0.23
Southeast Asians	**-1.20**	**-1.81, -0.59**	-0.19	-0.69, 0.31	-0.23	-0.49, 0.03
Other East Asians	-0.49	-1.23, 0.24	-0.27	-0.89, 0.36	--[b]	--

[a] Adjusted for age at baseline, education and income; [b] Sample size was too small to calculate estimate; bold indicates result different from 0 at p<0.05

Table 4.3. Differences (95% CI) in BMI change by age groups at immigration[a]

	BMI change between ages 30 & 40		BMI change between ages 40 & 50		BMI change between ages 50 & 60	
	Estimate	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
ALL ASIANS						
19 – 30 years	REF		REF		REF	
30 – 40 years	0.08	-0.32, 0.49	-0.10	-0.45, 0.26	0.21	-0.53, 0.95
40 – 50 years	**-0.45**	**-0.74, -0.15**	0.01	-0.31, 0.32	**0.55**	**0.02, 1.07**
50 – 60 years	**-0.48**	**-0.85, -0.11**	-0.35	-0.81, 0.12	0.36	-0.19, 0.92
60 – 68 years	-0.81	-1.74, 0.13	**-0.60**	**-1.03, -0.18**	0.70	-0.06, 1.47
CHINESE						
19 – 30 years	REF		REF		REF	
30 – 40 years	-0.08	-0.50, 0.33	-0.26	-0.66, 0.13	0.24	-0.80, 1.29
40 – 50 years	-0.29	-0.71, 0.14	0.06	-0.33, 0.45	**0.68**	**0.12, 1.24**
50 – 60 years	-0.22	-0.77, 0.33	-0.35	-1.03, 0.33	0.42	-0.12, 0.95
60 – 68 years	-0.09	-1.00, 1.18	-0.22	-0.78, 0.33	**1.09**	**0.18, 2.00**
SOUTHEAST ASIANS						
19 – 30 years	REF		REF		REF	
30 – 40 years	0.50	-0.32, 1.31	0.21	-0.44, 0.86	0.17	-0.90, 1.25
40 – 50 years	**-0.71**	**-1.13, -0.28**	-0.08	-0.60, 0.44	0.39	-0.52, 1.31
50 – 60 years	**-0.80**	**-1.24, -0.36**	-0.28	-0.89, 0.32	0.39	-0.69, 1.46
60 – 68 years	**-2.31**	**-3.42, -1.20**	**-1.22**	**-1.65, -0.80**	0.18	-0.80, 1.17
OTHER EAST ASIANS						
19 – 30 years	REF		REF		REF	
30 – 40 years	-0.34	-1.82, 1.14	0.72	-0.56, 2.02	--[b]	--
40 – 50 years	0.38	-1.16, 1.92	0.42	-0.44, 1.28	0.83	-0.51, 2.16
50 – 60 years	-0.65	-1.23, 0.06	-0.02	-0.77, 0.74	**1.86**	**0.79, 2.93**
60 – 68 years	--[b]	--	--[b]	--	--[b]	--

[a] Adjusted for age at baseline, education and income; [b] Sample size was too small to calculate estimate; bold indicates a statistically significant difference from reference group at $p<0.05$; grey shading indicates that at these time points participants resided in Asia

Table 4.4. Differences (95% CI) in BMI change by calendar year at immigration[a]

	BMI change between ages 30 & 40		BMI change between ages 40 & 50		BMI change between ages 50 & 60	
	Estimate	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
ALL ASIANS						
1977 – 1986	-0.06	-0.46, 0.34	-0.17	-0.73, 0.38	0.01	-0.76, 0.78
1987 – 1991	-0.03	-0.47, 0.40	-0.14	-0.71, 0.44	0.06	-0.74, 0.85
1992 – 1997	-0.47	-0.97, 0.04	-0.23	-0.85, 0.40	-0.03	-0.85, 0.80
After 1997	REF		REF		REF	
CHINESE						
1977 – 1986	-0.35	-0.90, 0.19	0.06	-0.56, 0.69	-0.05	-0.98, 0.87
1987 – 1991	-0.27	-0.85, 0.32	0.04	-0.61, 0.70	-0.01	-0.95, 0.94
1992 – 1997	-0.64	-1.35, 0.08	0.25	-0.50, 1.00	-0.40	-1.37, 0.57
After 1997	REF		REF		REF	
OTHER EAST ASIANS						
1977 – 1986	0.82	-0.17, 1.80	0.45	-0.51, 1.41	0.34	-0.47, 1.15
1987 – 1991	0.01	-1.10, 1.11	0.81	-0.45, 2.07	-0.13	-1.20, 0.93
1992 – 1997	REF		REF		REF	
SOUTHEAST ASIANS						
1977 – 1986	**0.51**	**0.06, 0.97**	-0.67	-1.65, 0.30	0.20	-1.10, 1.50
1987 – 1991	0.52	-0.04, 1.08	-0.53	-1.54, 0.47	0.20	-1.14, 1.54
1992 – 1997	0.02	-0.60, 0.64	-1.00	-2.05, 0.06	0.39	-1.01, 1.78
After 1997	REF		REF		REF	

[a] Adjusted for age at baseline, education and income; [b] No Other East Asian participants immigrated after 1997; bold indicates a statistically significant difference from reference group

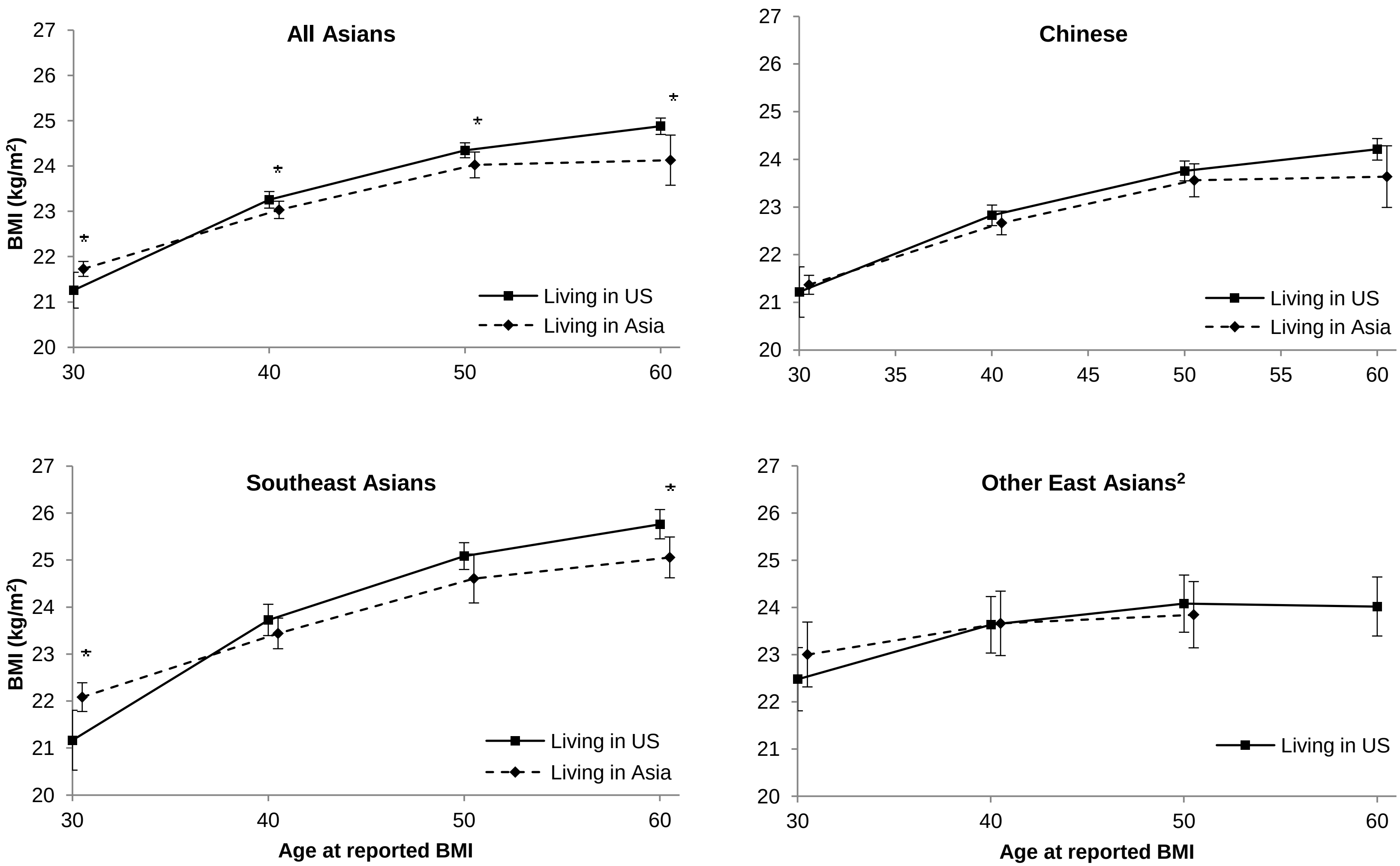

Figure 4.1. Adjusted[1] mean BMI (95% CI) at ages 30, 40, 50 and 60 comparing Asians living in Asia to Asians living in the US (point estimates for Asian residence are shifted to the right for display)
* Significantly different with $p<0.05$; [1] Adjusted for age at baseline, income and education; [2] No participant with BMI information at age 60 when living in Asia

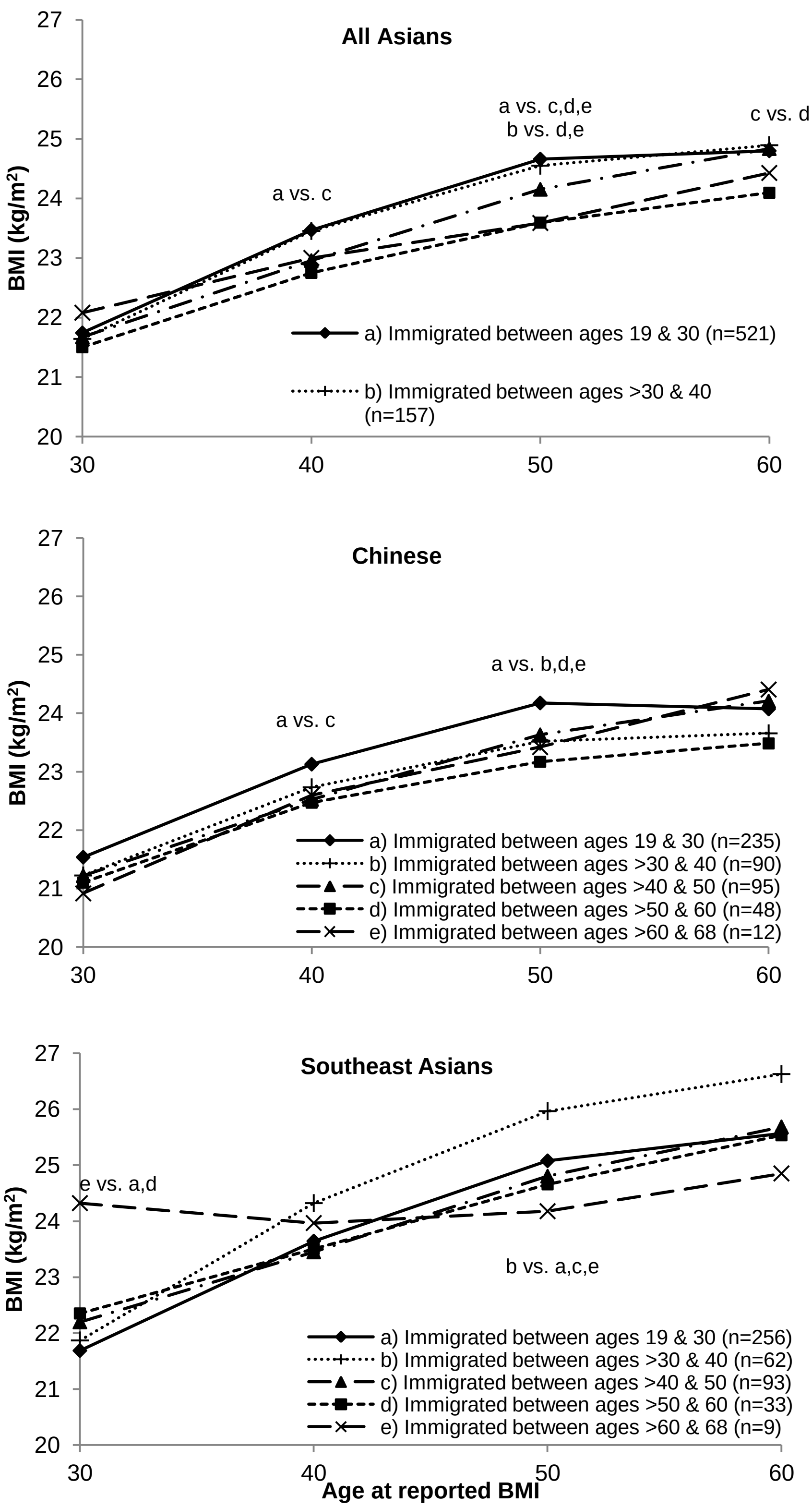

Figure 4.2. Adjusted[1] mean BMI at ages 30, 40, 50 and 60 by age at immigration

[1] Adjusted for age at baseline, income and education

Superscripts indicate statistically significant BMI differences between groups

V. LONGITUDINAL STUDY OF ACCULTURATION AND CHANGES IN BODY MASS INDEX AMONG ASIAN AMERICAN MEN

A. Abstract

Background: Cross-sectional studies examining the association between Western acculturation and BMI in Asians have been inconsistent, and studies on BMI change are lacking.

Objective: This study examined the associations between indicators of acculturation (generational status, length of US residence and age at immigration) and overweight (BMI $\geq 25 kg/m^2$) as well as 5-year BMI changes in 7,073 Chinese, Japanese, Korean, Filipino and Vietnamese men who lived in the US and were 44-71 years old at baseline of the California Men's Health Study (2002-2003).

Methods: Indicators of acculturation were reported at baseline. Repeated clinical measures of BMI were extracted from electronic health records (2005-2012).

Results: Using generalized estimating equations we found that lower generational status, shorter duration of US residence and older age at immigration were inversely associated with being overweight. However, analysis of BMI curves using linear mixed models showed that shorter length of US residence and older age at immigration were associated with larger 5-year increases in BMI.

Conclusions: Asian immigrants who were less acculturated had larger BMI increases as they became more acculturated, but had not achieved overweight status. Healthy weight interventions among Asians immigrants may be most effective when targeting weight maintenance early in the process of acculturation.

B. Background

Asians living in the US (Asian Americans) have a higher prevalence of overweight and obesity compared to Asians living in their ancestral countries [4,23]. These differences may be explained by exposure to a Western environment and acculturation, the process of adopting cultural traits of the host country [111]. However, cross-sectional studies examining the association between acculturation and body mass index (BMI) in Asian immigrants to Western countries have been inconsistent. Some studies found no association [46,51,58], while others found a positive association [66,68-71]. The authors of most studies combined all Asians and do not account for potential heterogeneity between Asian subgroups [72]. Additionally, BMI examined in cross-sectional studies might have been the same since pre-migration. Longitudinal studies on BMI change could clarify the previous contradictory results by assuring that the observed changes in BMI associated with different levels of acculturation occurred after immigration.

The obesity epidemic in the US has been linked to consumption of energy-dense foods and physical inactivity, characteristics of an obesogenic environment [112]. Acculturation to these norms may have detrimental effects on the health of Asian immigrants [50]. A pioneering study of the health consequences of American acculturation in Asians is the Honolulu Heart Program, which approximately 50 years ago recruited 8,006 men of Japanese ancestry living in Hawaii [58,59]. A higher level of maintenance of Japanese culture, measured using three self-reported scales (culture of upbringing, current cultural assimilation and current social assimilation), was related to lower levels of BMI in a cross-sectional analysis (26 vs. 23kg/m^2 in lowest vs. highest quartile, P<0.05). Contrary to expectation, Japanese born in Hawaii did not have a significantly different mean BMI compared to those born in Japan. This may be because data were collected prior to the US obesity epidemic, which was first detected in the late 70's[56]. More recently, there have been huge transitions in the economy, lifestyles and obesity prevalence in many Asian countries [57]. Therefore, early research has limited application to recent waves of Asian immigrants to the US.

Our study determined associations of measures of acculturation (generation, length of US residence and age at immigration), indicating an immigrant's exposure to the Western environment, with overweight ($\geq$25kg/m^2) and longitudinal changes in BMI among Asian men. We also sought to examine potential heterogeneity within the Asian population by analyzing results for Asian subgroups separately (Chinese, Japanese, Koreans, Filipino and Vietnamese). To our knowledge this is the first study that has used serial assessments of measured BMI to examine the impact of Western acculturation in Asians.

C. Methods

1. *Study population*

The California Men's Health Study is a prospective cohort initiated by Kaiser Permanente Northern and Southern California in 2002-2003[78]. Eligible participants were males aged 44-71 years who had been Kaiser Permanente members for at least one year prior to study enrollment. The baseline questionnaire collected information on demographics, acculturation and anthropometrics and was completed by 8,634 Asian men (Chinese, Japanese, Korean, Filipino, Vietnamese). Questionnaire data were linked with participants' electronic health records between 2005-2012 to extract information on weight and height measured at clinic visits.

We excluded participants with missing health records (n=528 Chinese, 154 Japanese, 48 Korean, 388 Filipino, 110 Vietnamese) and those with missing measured height (n=1 Chinese).

We also excluded participants with >73 clinic visits within the 8 year follow-up (top 1% of sample). These participants are assumed to have an illness that requires them to frequently visit their physician and may have experienced illness-related weight changes (n=16 Chinese, 14 Japanese, 4 Koreans, 23 Filipino, 2 Vietnamese). Finally, we excluded participants with missing information on income or education (n=141 Chinese, 40 Japanese, 4 Korean, 72 Filipino, 16 Vietnamese) leading to 3,325 Chinese, 1,088 Japanese, 263 Korean, 1,875 Filipino and 522 Vietnamese included in the analyses. This study was approved by the Institutional Review Boards of Kaiser Permanente Northern and Southern California and this secondary analysis was approved by Kaiser Permanente and University of North Carolina at Chapel Hill Non-Biomedical Institutional Review Boards on research involving human subjects.

2. *Measures*

BMI. Baseline BMI was calculated from self-reported weight and height. We extracted clinically measured weight and height from participants' health records (2005-2012). Height was not measured at all clinic visits and, on average, participants had 15 height measurements. To calculate BMI (kg/m^2) for each year of follow-up we used each participant's average height from his first 15 clinic visits and average weight from each clinic visit within a year. Follow-up and definition of a year started with a participant's first weight measurement. The use of average annual weight avoids spurious influences from minor weight fluctuations. Each participant could have up to 8 BMI measurements. We dichotomized BMI into normal weight (18.5-24.9kg/m^2) and overweight ($\geq$25kg/m^2). In secondary analyses we also used the Asian-specific cutpoint for overweight ($\geq$23kg/m^2)[86]. We calculated BMI changes between clinic visits and scaled them to

5-year changes. Time was calculated as the average age at each weight measurement within a year.

Indicators of acculturation. Information on acculturation was reported at baseline. Place of birth of participants and their parents was used to determine immigrant generation. First-generation includes foreign-born participants with foreign-born parents, second-generation includes US-born participants with at least one foreign-born parent and third-generation includes US-born participants with US-born parents.

Among foreign-born participants (n=4,991) we also examined length of US residence and age at immigration. Duration of US residence was categorized into <10, 11-25 and >25 years. Age at immigration was calculated by subtracting duration of US residence from baseline age. Since duration of residence was assessed in categories we estimated an age interval during which participants immigrated. We categorized participants into ≤40 and >40 years at immigration if both the lowest and highest possible age at immigration fell into the same category. In sensitivity analyses, we assigned observations with missing age at immigration to the highest possible age and then to the lowest possible age. This did not change our conclusions and we feel confident that these exclusions did not bias our results.

3. *Statistical analyses*

We used generalized estimating equation models to calculate odds ratios (OR) and 95% confidence intervals (CI) of being overweight comparing different levels of acculturation. Continuous BMI was analyzed using linear mixed models to estimate parameters of a 2-level hierarchical linear model[90] for BMI curves to calculate the difference in 5-year BMI change

(95% CI) across different levels of acculturation. Separate models for each measure of acculturation were estimated. In the level 1 models we regressed BMI on linear, continuous age at BMI measurement. In the level 2 models we predicted the level 1 coefficients from the specific measure of acculturation and baseline age, annual household income (<$40 000, $40 000-59 999, $60 000-79 999, ≥$80 000) and education (≤high school, vocational/some college, college graduate, graduate degree). The error terms followed a normal distribution with a mean of 0. To determine if the observed associations were driven by differential BMI at baseline we also adjusted the level-2 models for self-reported BMI at baseline in sensitivity analyses.

In all analyses we used an autoregressive order 1 covariance structure[88,89] and fit separate models for each indicator of acculturation. The most acculturated category was used as reference (i.e. third-generation, >25 years in the US and age at immigration of ≤40). An interaction by Asian subgroups indicated significant heterogeneity in the associations between acculturation and BMI over time, but not overweight. Thus, we presented results for all Asians combined for overweight, but subgroups-specific results for BMI change over time.

In analyses of length of US residence and age at immigration among foreign-born Asians we also used US-born Asians as reference to determine at which level of acculturation the risk of increased BMI among foreign-born Asians is different from or similar to US-born Asians. Vietnamese were not examined separately in this analysis of BMI change since all Vietnamese participants were foreign-born. We used SAS Statistical Software (proc genmod and proc mixed), version 9.3 (Cary, NC). All tests and *P*-values were two-sided and considered statistically significant at α=0.05.

D. Results

At baseline, participants of each Asian subgroup were on average between 58 and 60 years old (Table 5.1). Less than 10% of Japanese, Koreans and Filipinos, but almost one-quarter of Vietnamese had less than a high school degree. Similarly, one-third of Vietnamese had an annual household income of <$40,000, while the proportion was lower in the other subgroups. The majority of Chinese, Koreans, Filipinos and Vietnamese were foreign-born, while only 16.5% of Japanese were foreign-born. With the exception of Vietnamese, the majority of foreign-born participants from each Asian subgroup had resided in the US for >25 years and immigrated at age ≤40. The majority of foreign-born Vietnamese had lived in the US for 11-25 years and immigrated at age ≤40.

Lower generational status was associated with lower odds of overweight (Table 5.2). Among all Asians combined, first-generation men had 50% lower odds compared to third-generation men (OR=0.50, 95% CI: 0.44, 0.57) and 45% lower odds compared to second-generation men (OR=0.55, 95% CI: 0.48, 0.64, data not shown). In contrast, second-generation Asians had similar odds of overweight as third-generation participants.

Among foreign-born Asians, a shorter length of US residence was associated with lower odds of overweight (Table 5.2). Compared to Asians living in the US for >25 years, those living in the US for 11-25 years had 30% lower odds (OR=0.70, 95% CI: 0.63, 0.78) and those living in the US for <10 years had 36% lower odds (OR=0.64, 95% CI: 0.51, 0.80). Asians who immigrated <10 years ago were not significantly different from those who immigrated between 11-25 years ago (data not shown). Since length of US residence and age at immigration are closely related measures, the results for age at immigration are very similar (Table 5.2). Older age at immigration was associated with lower odds of overweight. Asians who immigrated after age 40 had 15% lower odds (OR: 0.85; 95% CI: 0.71, 1.01), although only marginally significant (*P*=0.07). Using 23kg/m^2 as a cutpoint for overweight only slightly attenuated these results (Table 5.3). First-generation Asians and especially those who resided in the US for ≤25 years still had significantly lower odds of overweight compared to their respective reference category.

Foreign-born Asians never reached similar odds of overweight as US-born Asians (Table 5.4). Compared to US-born Asians, those who were foreign-born had significantly lower odds irrespective of their level of acculturation indicating that being born in Asia may have a protective effect against exposure to US norms of behaviors and obesogenic influences.

Five-year BMI change did not differ by generational status among all Asians combined (Wald test *P*=0.47), however, findings differed by Asian subgroups (Table 5.5). Compared to third-generation US-born participants, first-generation foreign-born Chinese had a 0.10 kg/m^2 *lower* increase in BMI over 5 years (95% CI: -0.21, 0.00), while first-generation foreign-born Koreans had a 1.54 kg/m^2 *higher* 5-year increase in BMI (95% CI: 0.91, 2.16). Furthermore, among foreign-born Asians, shorter length of US residence was associated with larger 5-year increases in BMI. Compared to Asians who have lived in the US for >25 years, those who have lived in the US 11-25 years and <10 years had 0.08 kg/m^2 (95% CI: 0.02, 0.14) and 0.18 kg/m^2 (95% CI: 0.04, 0.31) larger 5-year BMI changes, respectively. A similar trend was observed among Chinese and Filipinos. Older age at immigration was also associated with larger increases in BMI. Asians who immigrated at >40 years had a 0.17kg/m^2 (95% CI: 0.07, 0.27) larger 5-year increase in BMI compared to Asians who immigrated at ≤40 years. Findings were similar in Japanese and Koreans, but were most pronounced in Filipinos. After additional adjustment for BMI at baseline these results were attenuated among all Asians combined and among subgroups

(Table 5.6). Compared to their respective reference group, the lower increase in BMI among first-generation Chinese and the higher increase in BMI among first-generation Filipino who have lived in the US for <10 years was no longer statistically significant, while the higher 5-year BMI increase among first-generation Koreans was attenuated to 0.79 kg/m^2 (95% CI: 0.24, 1.35).

Finally, compared to US-born Asians, those who have lived in the US for <10 or 11-25 years, had significantly larger 5-year increases in BMI by 0.14 kg/m^2 (95% CI: 0.01, 0.28) and 0.07 kg/m^2 (95% CI: 0.00, 0.14), respectively, while Asians who have lived in the US for >25 years had a similar 5-year BMI change (Table 5.7). Among Koreans, first-generation, foreign-born individuals had significantly higher 5-year increases in BMI independent of their length of US residence compared to US-born Koreans. In contrast, foreign-born Chinese had lower 5-year BMI increases than US-born Chinese. Only the estimate for those who have lived in the US for >25 years was statistically significant (-0.11 kg/m^2, 95% CI: -0.20, -0.03). The results for age at immigration were similar to those of length of US residence.

E. Discussion

It has been hypothesized that Western acculturation is associated with higher BMI, but previous studies have been inconsistent[46,51,58,66,68-71]. Our longitudinal study provided further insight as it allowed the examination of BMI change. First-generation, foreign-born Asian men had a healthier BMI than second- or third-generation, US-born Asian men, even after being exposed to the Western environment for more than 25 years. Foreign-born Asian men rapidly gained weight during their first 25 years in the US, yet they never reached the same level of overweight as their US-born counterparts due to leveling off of weight gain after 25 years. A meta-analysis examining the association between Western society and hypertension also found that the largest impact of acculturation on health occurred at the time of initial contact with the new culture[113].

We found substantial heterogeneity within the Asian population. Some subgroups, such as Filipinos and Koreans, were at higher risk of weight gains due to acculturation than Chinese suggesting that BMI curves differ by Asian subpopulation. The estimates were attenuated after additional adjustment for BMI at baseline likely because less acculturated Asians had lower BMI at baseline than more acculturated Asians. Specifically, first-generation Chinese had an average BMI of 24.4 kg/m^2, while third-generation Chinese had a BMI of 26.2 kg/m^2 (24.6 and 27.8 kg/m^2 among Koreans, respectively). However, adjustment for baseline BMI when examining BMI change is still controversial[114]. Acculturation might have had a smaller impact on BMI change among Chinese since China has undergone a more rapid rate of Westernization compared to Japan or Korea[57]. Thus, Chinese might have already experienced substantial increases in BMI prior to migration to the US and were, thus, less susceptible to exposure to the US Western environment[115].

Compared to US-born Asians, foreign-born Asians were less likely to be overweight irrespective of how long they have been in the US or at what age they immigrated. Place of birth rather than length of exposure to the Western environment might be a better predictor of being overweight. Our estimates of the negative association between being foreign-born and overweight among all Asian subgroups combined agreed, except for subgroup analyses, with two previous cross-sectional studies from Kaiser Permanente Northern California where data was collected much earlier than the current study. Klatsky *et al.* included 13,031 Asians (1978-1985) and found that being foreign-born significantly lowered the odds of having a BMI $\geq$24.4kg/m^2 in Chinese, Japanese, Filipino and other Asian men[68]. The second study among 801 Asians (1996-

2001) found that, compared to their US-born counterparts, foreign-born Chinese and multiple-race Asians were significantly less likely to have a BMI >25kg/m^2, but not foreign-born Japanese, Filipinos or other Asians[66]. However, that study suffered from small sample sizes within each ethnic subgroup.

Using length of US residence as an indicator of acculturation among 1,651 Central Asians and 2,139 Southeast Asians from the National Health Interview Survey, Oza-Frank *et al.* found that prevalence of overweight increased with length of US residence for Central Asians, but not for Southeast Asians[69]. In contrast, two other studies among Asian immigrants in Canada and the US did not find a trend between length of residence in the host country and overweight[46,70]. A reason for these contradictory findings might be that heterogeneous Asian subgroups were combined, but may experience very different environments and levels of Westernization in their home countries, which can influence BMI levels observed after immigration to the US[73].

This present study builds on previous research examining whether self-reported longitudinal BMI patterns differed prior to immigration when Asian men still lived in Asia and after immigration when Asian men lived in the US (n=1,549; see Chapter IV). Age-related increases in BMI were lower for Asians who still lived in Asia compared to those who already immigrated to the US at specific ages, especially between ages 30-40 (Asia-US: -0.69kg/m^2; 95% CI: -1.08, -0.30). Additionally, larger increases in BMI were observed after immigration to the US, especially among those who immigrated to the US at an earlier age (before age 40). Our current study expands on this research by examining measured BMI changes across different levels of acculturation when Asian Americans lived in the US and by determining that BMI increases with increasing exposure to the Western environment.

In our study we were not able to determine the underlying factors that could have contributed to the differential changes in BMI among Asian immigrants. Acculturation likely leads to changes in lifestyle upon immigration, which subsequently can influence BMI. Other studies have demonstrated that after immigration to the US, Chinese, Japanese and Koreans increase their intake of cholesterol, saturated fat, sweets, dairy and fruit, but decrease their consumption of traditional foods, meat and meat alternatives and vegetables[98,116,117]. With increasing level of acculturation (measured as length of residence in Canada) portion sizes, frequency of dining out and consumption of convenience foods increases among Chinese[118]. Physical activity tends to decrease upon immigration to a Western country[99], but increases as Asian immigrants have lived longer in the US and become more acculturated[35,119,120].

Strengths of this study include determining heterogeneity by country of origin in the association between acculturation and BMI change. Additionally, we had access to information on clinically measured BMI over a follow-up of 8 years. We used generational status, length of US residence and age at immigration as measures of exposure to a Western obesogenic environment. These factors are commonly used proxies, but might not fully capture the multidimensional influences of acculturation. Since acculturation is such a complex phenomenon that cannot be captured in a simple quantitative measure, our goal was to use valid and reliable indicators that measure exposure to the US environment. The measures of acculturation used here are highly correlated with more comprehensive acculturation scales[121]. Length of residence has repeatedly been shown to have high levels of validity and reliability[72,122,123]. The categories of length of US residence and age at immigration we used were broad. Unfortunately, sample size limitations did not allow us to use smaller categories. Our results might not be generalizable to all Asian immigrants to the US since all participants were members of Kaiser Permanente, had health insurance and were residents of California. Our study population had slightly higher levels of education and income compared to the general Asian population in the US[106]; the proportion of individuals with less than a high school degree was 20% in the 2000 census compared to 15% in our study, while the proportion of individuals with an annual household income of <$40,000 was 37% and 22%, respectively. Immigrants to the US are a self-selected group and reasons for migration might have differed by Asian subgroups. Additionally, our sample was limited to Asian men. Men tend to be more negatively affected by acculturation than women as they are more likely to be in the workforce, which is associated with increased exposure to the host culture[79]. The differences in BMI changes by level of acculturation observed in our study are quite small. However, these changes can add up over time and any increase in BMI, even within the normal BMI range, has been associated with elevated risk of diabetes and cardiovascular disease (CVD)[124,125] and should be avoided. Additionally, Asians have higher risk of CVD at a lower BMI than Caucasians[110] likely because they have more body fat and less muscle at the same BMI level[5,6,8]. Thus, excess increases in BMI might have more harmful effects on health in Asians than other ethnic groups. This study makes an important contribution to the literature by showing differences in BMI by levels of acculturation longitudinally and across Asian subpopulations. The results greatly enhance our understanding of overweight risk in Asian Americans by pointing out that foreign-born Asian immigrants and especially those who recently immigrated are particularly susceptible to excess increases in BMI. Interventions focused on weight maintenance need to be targeted towards new immigrants when immigrants are most vulnerable to the pressures of acculturation. To further explain these weight gain patterns, future studies need to evaluate differences in environments in which foreign-born Asians live and assess different levels of access to traditional foods and physical activity.

Table 5.1. Characteristics of Asian men in the California Men's Health Study (2002-2012)

Characteristics	All Asians (n=7,073)	Chinese (n=3,325)	Japanese (n=1,088)	Korean (n=263)	Filipino (n=1,875)	Vietnamese (n=522)
Number of observations of measured BMI	31,895	14,766	5,038	1,224	8,565	2,302
Age at baseline in years [mean (SD)]	57.9 (7.1)	57.6 (7.2)	59.4 (7.1)	60.2 (6.6)	57.5 (6.8)	57.5 (6.8)
Clinically measured BMI in kg/m^2 [mean (SD)]	25.9 (3.7)	25.3 (3.6)	26.9 (3.8)	25.0 (3.1)	27.1 (3.8)	24.5 (3.0)
Education [n (%)]						
≤High school	996 (14.1)	570 (17.1)	106 (9.7)	22 (8.4)	184 (9.8)	114 (21.8)
Some college	1,957 (27.7)	784 (23.6)	319 (29.3)	45 (17.2)	621 (33.1)	188 (36.0)
College graduate	2,368 (33.5)	917 (27.6)	357 (32.8)	110 (41.8)	869 (46.4)	115 (22.0)
Graduate degree	1,752 (24.8)	1,054 (31.7)	306 (28.1)	86 (32.6)	201 (10.7)	105 (20.1)
Annual household income [n (%)]						
<\$40,000	1,452 (20.5)	668 (20.1)	144 (13.2)	62 (23.8)	404 (21.6)	174 (33.3)
\$40,000-59,999	1,405 (19.9)	602 (18.1)	214 (19.7)	58 (21.8)	412 (22.0)	119 (22.8)
\$60,000-79,999	1,246 (17.6)	537 (16.2)	212 (19.5)	46 (17.2)	360 (19.2)	91 (17.4)
≥\$80,000	2,970 (42.0)	1,518 (45.7)	518 (47.6)	97 (37.2)	699 (37.3)	138 (26.4)
Generational status [n (%)]						
1st generation	4,991 (70.6)	2,304 (69.1)	179 (16.5)	242 (78.2)	1,749 (93.5)	517 (99.0)
2nd generation	793 (11.2)	511 (15.4)	191 (17.6)	9 (3.4)	82 (4.4)	0
3rd generation	1,260 (17.8)	494 (15.0)	715 (65.7)	11 (4.2)	40 (2.1)	0
Missing	29 (0.4)	16 (0.5)	3 (0.3)	1 (0.4)	4 (0.2)	5 (1.0)
Length of US residence among foreign-born [n (%)]						
<10 years	326 (6.5)	162 (7.0)	2 (1.1)	2 (0.8)	131 (7.5)	29 (5.6)
11-25 years	1,975 (39.6)	903 (39.2)	21 (11.7)	77 (31.8)	692 (39.6)	282 (54.5)
>25 years	2,677 (53.6)	1,234 (53.6)	156 (87.2)	162 (66.9)	920 (52.6)	205 (39.7)
Missing	13 (0.3)	5 (0.2)	0	1 (0.4)	6 (0.3)	1 (0.2)
Age at immigration among foreign-born [n (%)]						
≤40 years	3,017 (60.4)	1,357 (58.9)	140 (78.2)	152 (62.8)	1,079 (61.7)	289 (55.9)
>40 years	778 (15.6)	372 (16.1)	4 (2.2)	18 (7.4)	285 (16.3)	99 (19.1)
Missing	1,196 (24.0)	575 (25.0)	35 (19.6)	72 (29.8)	385 (22.0)	129 (25.0)

n = sample size; SD = standard deviation

Table 5.2. Odds Ratio (95% Confidence Interval) of Overweight (BMI ≥25.0 kg/m^2) Across Different Levels of Acculturation Among all Asians, California Men's Health Study (2002-2012)[a]

Characteristics	All Asians (n=7,073)		
	n[b]	**OR**	**95% CI**
Among entire sample			
Generational status			
1st generation	11,657	**0.50**	**0.44, 0.57**
2nd generation	2,387	0.90	0.76, 1.08
3rd generation	3,917	REF	
Among foreign-born Asians			
Length of US residence			
<10 years	668	**0.64**	**0.51, 0.80**
11-25 years	4,481	**0.70**	**0.63, 0.78**
>25 years	12,809	REF	
Age at Immigration			
≤40 years	7,297	REF	
>40 years	1,643	0.85	0.71, 1.01

BMI = body mass index; CI = confidence interval, n = sample size; OR = odds ratio; REF = reference; bold font indicates statistically significant different odds from reference group at $p<0.05$; [a] Adjusted for age at baseline, education and income; [b] Number of overweight observations, participants can have multiple observations; Bold indicates a statistically significant difference from reference group at $P<0.05$

Table 5.3. Odds Ratio (95% Confidence Interval) of Overweight (BMI ≥23.0 kg/m^2) Across Different Levels of Acculturation Among all Asians, California Men's Health Study (2002-2012)[a]

Characteristics	All Asians (n=7,073)		
	n[b]	OR	95% CI
Among entire sample			
Generational status			
1st generation	17,355	**0.54**	**0.46, 0.64**
2nd generation	3,099	0.89	0.70, 1.13
3rd generation	4,944	REF	
Among foreign-born Asians			
Length of US residence			
<10 years	1,026	**0.73**	**0.57, 0.94**
11-25 years	6,666	**0.79**	**0.70, 0.89**
>25 years	17,717	REF	
Age at Immigration			
≤40 years	10,597	REF	
>40 years	2,515	0.86	0.70, 1.05

BMI = body mass index; CI = confidence interval, n = sample size; OR = odds ratio; REF = reference; bold font indicates statistically significant different odds from reference group at p<0.05; [a] Adjusted for age at baseline, education and income; [b] Number of overweight observations, participants can have multiple observations; Bold indicates a statistically significant difference from reference group at *P*<0.05

Table 5.4. Odds Ratio (95% Confidence Interval) of Overweight (BMI ≥25.0 kg/m^2) Across Different Levels of Acculturation Among all Asians Compared to US-Born Asian Men, California Men's Health Study (2002-2012)[a]

Characteristics	**All Asians** (n=7,073)		
	n[b]	**OR**	**95% CI**
Length of US residence			
<10 years	661	**0.43**	**0.34, 0.55**
11-25 years	4,478	**0.49**	**0.43, 0.56**
>25 years	6,536	**0.55**	**0.49, 0.61**
US-born	6,304	REF	
Age at Immigration			
US-born	6,304	REF	
≤40 years	7,297	**0.55**	**0.49, 0.62**
>40 years	1,643	**0.48**	**0.40, 0.57**

BMI = body mass index; CI = confidence interval, n = sample size; OR = odds ratio; REF = reference; bold font indicates statistically significant different odds from reference group at p<0.05; [a] Adjusted for age at baseline, education and income; [b] Number of overweight observations, participants can have multiple observations; Bold indicates a statistically significant difference from reference group at *P* <0.05

Table 5.5. Difference (95% Confidence Interval) in 5-Year BMI Change Across Different Levels of Acculturation Among all Asians and Asian subgroups, California Men's Health Study (2002-2012)[a]

Characteristics	All Asians (n=7,073)		Chinese (n=3,296)		Japanese (n=1,088)	
	BMI change	**95% CI**	**BMI change**	**95% CI**	**BMI change**	**95% CI**
Among entire sample						
Generational status						
1st generation	0.04	-0.03, 0.11	**-0.10**	**-0.21, 0.00**	0.01	-0.19, 0.20
2nd generation	0.01	-0.09, 0.10	-0.05	-0.18, 0.07	-0.18	-0.38, 0.03
3rd generation	REF		REF		REF	
Among foreign-born Asians						
Length of US residence						
<10 years	**0.18**	**0.04, 0.31**	0.14	-0.04, 0.316	0.99	-1.65, 3.63
11-25 years	**0.08**	**0.02, 0.14**	**0.09**	**0.00, 0.18**	-0.33	-0.96, 0.31
>25 years	REF		REF		REF	
Age at Immigration						
≤40 years	REF		REF		REF	
>40 years	**0.17**	**0.07, 0.27**	-0.002	-0.01, 0.01	0.98	-0.95, 2.91

	Korean (n=261)		Filipino (n=1,871)		Vietnamese (n=516)	
	BMI change	**95% CI**	**BMI change**	**95% CI**	**BMI change**	**95% CI**
Among entire sample						
Generational status	**1.54**	**0.91, 2.16**	0.01	-0.40, 0.41	[b]	
1st generation	0.40	-0.43, 1.24	0.07	-0.39, 0.54	[b]	
2nd generation	REF		REF		REF	
3rd generation						
Among foreign-born Asians						
Length of US residence						
<10 years	0.01	-1.42, 1.44	**0.22**	**0.01, 0.45**	-0.09	-0.52, 0.35
11-25 years	0.11	-0.18, 0.39	0.09	-0.03, 0.20	0.10	-0.08, 0.28
>25 years	REF		REF		REF	
Age at Immigration						
≤40 years	REF		REF		REF	
>40 years	0.15	-0.48, 0.78	**0.22**	**0.04, 0.39**	-0.03	-0.18, 0.40

BMI = body mass index; CI = confidence interval, n = sample size; REF = reference; bold font indicates a statistically significant difference from reference group at $p<0.05$; [a] Adjusted for age at baseline, education and income; [b] Sample size was too small to calculate estimate; Bold indicates a statistically significant difference from reference group at $P<0.05$

Table 5.6. Difference (95% Confidence Interval) in 5-Year BMI Change Across Different Levels of Acculturation Among all Asians and Asian subgroups with additional adjustment for baseline BMI, California Men's Health Study (2002-2012)[a]

Characteristics	**All Asians** (n=7,073)		**Chinese** (n=3,296)		**Japanese** (n=1,088)	
	BMI change	**95% CI**	**BMI change**	**95% CI**	**BMI change**	**95% CI**
Among entire sample						
Generational status						
1st generation	0.03	-0.02, 0.09	-0.05	-0.14, 0.04	-0.09	-0.25, 0.07
2nd generation	-0.03	-0.11, 0.05	-0.08	-0.19, 0.03	-0.14	-0.32, 0.04
3rd generation	REF		REF		REF	
Among foreign-born Asians						
Length of US residence						
<10 years	**0.12**	**0.00, 0.23**	0.06	-0.08, 0.21	0.69	-1.18, 2.56
11-25 years	**0.06**	**0.00, 0.11**	0.06	-0.01, 0.14	-0.38	-0.88, 0.11
>25 years	REF		REF		REF	
Age at Immigration						
≤40 years	REF		REF		REF	
>40 years	0.08	-0.01, 0.17	0.06	-0.06, 0.18	0.45	-0.97, 1.87

	Korean (n=261)		**Filipino** (n=1,871)		**Vietnamese** (n=516)	
	BMI change	**95% CI**	**BMI change**	**95% CI**	**BMI change**	**95% CI**
Among entire sample						
Generational status	**0.79**	**0.24, 1.35**	-0.14	-0.49, 0.22	[b]	
1st generation	-0.15	-0.90, 0.60	-0.15	-0.55, 0.25	[b]	
2nd generation	REF		REF		REF	
3rd generation						
Among foreign-born Asians						
Length of US residence						
<10 years	0.32	-1.05, 1.69	0.16	-0.05, 0.36	-0.13	-0.53, 0.26
11-25 years	0.14	-0.11, 0.40	0.04	-0.06, 0.15	0.08	-0.08, 0.25
>25 years	REF		REF		REF	
Age at Immigration						
≤40 years	REF		REF		REF	
>40 years	0.15	-0.43, 0.74	0.09	-0.07, 0.25	0.004	-0.27, 0.28

BMI = body mass index; CI = confidence interval, n = sample size; REF = reference; [a] Adjusted for age at baseline, education, income and self-reported baseline BMI; [b] Sample size was too small to calculate estimate; Bold indicates a statistically significant difference from reference group at P <0.05

Table 5.7. Difference (95% Confidence Interval) in 5-Year BMI Change Across Different Levels of Acculturation Among all Asians and Asian Subgroups Compared to US-Born Asians, California Men's Health Study (2002-2012)[a]

Characteristics	**All Asians** (n=7,073)		**Chinese** (n=3,296)		**Japanese** (n=1,088)	
	BMI change	**95% CI**	**BMI change**	**95% CI**	**BMI change**	**95% CI**
Among foreign-born Asians						
Length of US residence						
<10 years	**0.14**	**0.01, 0.28**	-0.01	-0.20, 0.17	1.10	-1.40, 3.60
11-25 years	**0.07**	**0.00, 0.14**	-0.04	-0.14, 0.06	-0.05	-0.62, 0.51
>25 years	0.00	-0.06, 0.06	**-0.11**	**-0.20, -0.03**	0.02	-0.17, 0.22
US-born	REF		REF		REF	
Age at Immigration						
≤40 years	REF		REF		REF	
>40 years	0.00	-0.06, 0.07	**-0.10**	**-0.19, -0.02**	0.05	-0.17, 0.27
US-born	**0.17**	**0.07, 0.27**	0.06	-0.08, 0.20	0.76	-0.92, 2.43

	Korean (n=261)		**Filipino** (n=1,871)	
	BMI change	**95% CI**	**BMI change**	**95% CI**
Among foreign-born Asians				
Length of US residence				
<10 years	1.52	-0.03, 3.07	0.12	-0.18, 0.42
11-25 years	**1.40**	**0.92, 1.88**	-0.01	-0.23, 0.21
>25 years	**1.27**	**0.83, 1.71**	-0.08	-0.30, 0.14
US-born	REF		REF	
Age at Immigration				
≤40 years	REF		REF	
>40 years	**1.38**	**0.69, 1.70**	-0.10	-0.32, 0.41
US-born	**1.19**	**0.67, 2.09**	0.15	-0.11, 0.41

BMI = body mass index; CI = confidence interval, n = sample size; REF = reference; bold font indicates a statistically significant difference from reference group at p<0.05; [a] Adjusted for age at baseline, education and income; All Vietnamese were 1st generation and are, thus, not included in this table; Bold indicates a statistically significant difference from reference group at *P*<0.05

VI. The Role of Body Mass Index in the Association Between Acculturation and Incident Type 2 Diabetes among Asian American Men

A. Abstract

Background: Exposure to an obesogenic Western environment has been hypothesized to increase type 2 diabetes risk among Asian Americans. Potential modifiable factors that mediate this association are unknown.

Objective: To determine the association between acculturation and incident diabetes in Asian Americans and to determine BMI's role as a mediator in this relationship.

Methods: This study included 5,346 Asians from the California Men's Health Study. Baseline information on acculturation (generation and length of US residence) was merged with participants' electronic health records to extract data on BMI measurements at clinic visits and diabetes diagnosis. Marginal structural Cox proportional hazard models were used to determine the total effect and the controlled direct effect (independent of BMI) of acculturation on incident diabetes.

Results: We identified 496 incident diabetes cases and a diabetes rate of 14.40 per 1,000 person-years (95% CI: 12.51, 16.57) after standardization to a BMI of 21 kg/m^2 and age 58.1 years. Contrary to our hypothesis, we observed an inverse total effect of acculturation on diabetes with more acculturated Asians having a lower risk of diabetes. After controlling for BMI this association was further strengthened.

Conclusion: Exposure to the US environment might protect Asian immigrants from diabetes risk factors other than BMI (e.g. access to chronic disease prevention efforts). BMI

explained only part of the association between acculturation and incident diabetes and future studies need to examine other modifiable factors (e.g. physical activity) that might mediate this association.

B. Background

Asians living in the US (Asian Americans) have double the risk of type 2 diabetes compared to Caucasians[10]. Asian Americans might be exposed to a dual burden that puts them at a disproportionately larger risk for diabetes. First, exposure to the American obesogenic environment, which is conducive to consumption of energy-dense foods and physical inactivity, fuels high levels of CVD-related risk in America including among highly susceptible Asian immigrant populations adapting to American norms[50]. Second, Asians have a high level of innate diabetes risk as they tend to have higher risk of morbidity at a lower BMI than other ethnic groups, likely because they have more abdominal fat at the same BMI level[5-8]. Immigrants seem to exceed the diabetes rate of their host country after immigration[27]. This could be partly explained through the effect of acculturation to an obesogenic environment (i.e. a cultural change from a traditional Asian lifestyle to a Western lifestyle when migrating from Asia to the US) on BMI as immigrants adapt to the host culture.

We previously showed that higher levels of acculturation were associated with larger increases in BMI (see Chapter V). We know of only one longitudinal study on acculturation (measured by place of birth) and diabetes, but this study suffered from small sample size (45 incident diabetes cases) and did not find an association[74]. Cross-sectional studies of prevalent diabetes have been inconsistent with one finding a positive association with place of birth[58], while others did not find an association between place of birth[62,126], length of US residence[60] or an acculturation score[61] and diabetes among Asian Americans.

There is a vast literature showing that diabetes risk increases with increasing BMI in Asians[127,128]. In addition, Asians tend to be more susceptible to diabetes at a lower BMI compared to other ethnic groups. We previously examined the impact of BMI on diabetes incidence in Asians living in Asia (n=5,980) compared to Caucasians living in the US (n=10,776)[129] and found that the risks for development of diabetes associated with elevated BMI were larger in Chinese living in China (n=5,980) compared with American Caucasians (n=10,776)[129]. The Multi-Ethnic Study of Atherosclerosis (MESA) also found that the slope of incident diabetes with BMI tended to be steeper in Chinese Americans compared to Caucasian Americans[130].

It is logical to hypothesize that changes in BMI at least partially explain the associations between acculturation and disease risk in Asian Americans, but this possibility has been inadequately investigated[39]. Previous studies considered BMI as a confounder rather than a mediator in the acculturation-diabetes association and compared models on the association between acculturation and diabetes without adjustment for current BMI to models with adjustment for BMI[58,61,74]. However, BMI is more likely a consequence of acculturation rather than a predictor and, thus, it is more likely a mediator in this relationship. In addition, covariate adjustment to assess mediation is only valid under several restrictive assumptions that are difficult to meet[131], and therefore this approach has significant potential for bias[75,76,132]. An alternative counterfactual-based approach has recently been proposed, which is valid under more general conditions[133]. The goal of this longitudinal study was to determine the association between acculturation and incident type 2 diabetes in Asian Americans and to assess BMI's role as a mediator in this relationship.

C. Methods

1. *Study population*

The California Men's Health Study was initiated in 2002 and eligible participants were 44 to 71 year old men who were members of Kaiser Permanente of Northern or Southern California[78]. The baseline data on demographics, socioeconomic status and acculturation were linked with participants' electronic health records (2005-2012) to extract information on measured BMI at each clinic visit and diagnosis of diabetes.

The California Men's Health Study included 8,634 Asians. We excluded participants with missing health records (n=1,228) or missing weight and height measurements (n=1). We also excluded participants with self-reported diabetes at baseline (n=1,295) and those whose diabetes diagnosis occurred prior to BMI measurements (n=561). Prevalence of diabetes was slightly higher among first-generation than second- or third-generation Asians (31.9% vs. 26.7% and 27.4%, respectively; Chi-square $p < 0.0001$). Finally, we excluded participants with missing information on education or income (n=203) and acculturation (n=28). After these exclusions 5,318 Asians were included in our analyses. This study was approved by the Institutional Review Boards of Kaiser Permanente Northern and Southern California and this secondary analysis was approved by Kaiser Permanente and University of North Carolina at Chapel Hill Non-Biomedical Institutional Review Boards on research involving human subjects.

2. *Measures*

Measure of acculturation. Acculturation was assessed in the baseline questionnaire. Information on participants' and their parents' place of birth was used to determine generational status. First-generation includes foreign-born participants with foreign-born parents, second-generation includes US-born participants with at least one foreign-born parent and third-generation includes US-born participants with US-born parents. Length of US residence among first-generation participants was categorized into <10, 11-25 and >25 years. We combined information on generational status and length of US residence into a comprehensive measure of acculturation[134]: first-generation and lived in the US <10 years, first-generation and lived in the US 11-25 years, first-generation and lived in the US >25 years, second-generation and third-generation.

Body mass index. Participants' health records provided information on measured weight and height at each clinic visit (2005-2012). Height was not consistently measured at all clinic visits and participants had, on average, 15 height measurements. We calculated BMI (kg/m^2) using each participant's average height from his first 15 clinic visits and average weight from each clinic visit within a year. The beginning of each year of observation started with a participant's first weight measurement. The use of average annual weight avoids spurious influences from minor weight fluctuations and resulted in up to 8 BMI measurements for each participant. To allow for non-linearity, we categorized BMI into underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) and obesity (≥30.0 kg/m^2).

Diabetes. Kaiser Permanente developed recommendations that guide primary care physicians for screening patients for type 2 diabetes. To identify type 2 diabetes cases we extracted data on membership, primary care utilization, laboratory tests and pharmaceutical use from health plan electronic databases from 2005-2012. Type 2 diabetes diagnoses were based on four automated health-plan data sources including pharmacy prescriptions for diabetes medications or supplies (insulin, sulfonylurea drugs, metformin, and blood glucose testing supplies), abnormal HbA_{1c} values (>6.7%) in regional laboratory files, primary or secondary hospital discharge diagnosis of diabetes, and emergency department visits for which a physician diagnosis of diabetes was listed[87]. Recommendations for screening tests were not weight related and time intervals for the screening tests were based on the health plans' clinical practice guidelines.

3. *Statistical analyses*

Poisson regression was used to calculate crude incidence rates and incidence rates standardized to a BMI of 21 kg/m^2 and age 58.1 years (mean age). The total effect of acculturation on incident type 2 diabetes was determined using Cox regression models with age as the time scale to determine the hazard ratio (HR) and 95% confidence interval (CI) of diabetes across different levels of acculturation using the category considered the most acculturated as the reference group (i.e., third-generation). The models were adjusted for age at baseline, education and income using inverse probability weighting as described below. There was no evidence for violation of the proportional hazards assumption, as assessed by visual inspection of ln(-ln(Survival)) plots.

We estimated the controlled direct effect of acculturation, independent of BMI, on risk of diabetes using inverse-probability (IP) weighted marginal structural models (MSM) outlined by VanderWeele (Figure 3.1.)[76,91]. The interpretation of the controlled direct effect is the association of acculturation on diabetes risk if BMI was set to a particular level; thus, we estimate controlled direct effects for the acculturation given each possible level of BMI. The validity of this model assumes counterfactual consistency (well defined exposures and mediators), positivity (each subject has the possibility of experiencing each exposure and mediator level) and exchangeability (no confounding between the exposure and the outcome as well as no confounding between the mediator and the outcome)[91,93]. The weights for the MSM were based on the variables BMI (*M*), acculturation (*A*) and confounders of the BMI-diabetes and acculturation-diabetes relationships (*C*, specified as age at baseline, income and education). The first set of (stabilized) weights, which blocks the pathway from acculturation to BMI (thereby isolating the direct effect of acculturation), and controls for BMI-diabetes confounders, are given by:

$$w_{1,i} = P(M_i = m_i | A_i = a_i)/P(M_i = m_i | A_i = a_i, C_i = c_i)$$

for individuals indexed by i, where lower case letters denote the observed value of the corresponding variable. The second set of weights, which controls for confounders of the acculturation-diabetes relationship, are based on acculturation (A) and confounders (C):

$$w_{2,i} = P(A_i = a_i)/P(A_i = a_i | C_i = c_i).$$

The probabilities in each of the above expressions were estimated using multinomial logistic regression models. Each individual’s final weight was then calculated as

$$w_i = w_{1,i} \times w_{2,i}.$$

The final IP weighted Cox MSM was fit using the above weights and terms for the main effects of acculturation (*A*), BMI (*M*) and the acculturation-BMI interaction. We additionally estimated the direct effects of acculturation pooled across levels of BMI, which assumes homogeneity of the effect of acculturation with respect to BMI. The total effect of acculturation was estimated using only main effects for acculturation and the second set of weights (w_2). These models were fit using the PHREG and GENMOD procedures in SAS version 9.3 (Cary, NC).

D. Results

Participants were on average 58.1 (SD: 7.1) years old at baseline and had a BMI of 25.5 kg/m^2 (SD: 3.5) during clinic visits (data not shown). More than half of participants were college graduates and had an income of ≥$60,000 (Table 6.1). The majority of Asians were first-generation (70%).

We identified 496 incident diabetes cases over a follow-up of 28,558 person-years. The overall crude diabetes rate, per 1,000 person-years, was 17.37 (95% CI: 15.84, 18.90) and decreased to 14.40 (95% CI: 12.51, 16.57) after standardization to BMI of 21 kg/m^2 and age of 58.1 years. The lowest crude diabetes incidence was observed among those who were younger, had a lower BMI, had a graduate degree and an income of ≥$60,000 (Table 6.1). Across levels of acculturation, Asians who were third-generation had the lowest crude incidence rate.

Compared to third-generation Asians, those with lower levels of acculturation had a higher rate of diabetes (Table 6.2). This association was especially pronounced for first-generation Asians who have lived in the US for 11-25 and >25 years. Compared to third-generation Asians, these groups had a 56% (95% CI: 1.18, 2.07) and 47% (95% CI: 1.12, 1.93) higher rate of diabetes.

Estimating the direct effects of acculturation pooled across levels of BMI (Table 6.2) showed that the association independent of BMI was slightly more pronounced among first-generation, but not second-generation participants likely because first-generation Asians had on average lower levels of BMI compared to second- or third-generation Asians (Table 6.3). Controlling for BMI strengthened the association especially for Asians in the lowest level of acculturation. Compared to third-generation Asians, first-generation Asians who have lived in the US for <10 years had a 66% (95% CI: 1.03, 2.68) higher rate of diabetes after controlling for BMI.

We found that the effect of acculturation on diabetes was heterogeneous across levels of BMI (Wald $p<0.0001$) and, therefore, we also estimated the interaction between acculturation and BMI. Lower levels of acculturation were most strongly associated with diabetes in Asians with a BMI of 18.5-24.9 kg/m^2 or ≥30 kg/m^2 (Table 6.4). When using a single referent group (overweight third-generation) the association was further strengthened in those with a BMI of ≥30 kg/m^2 indicating that the baseline risk of diabetes was increased in this BMI category compared to those with BMI of 25.0-29.9 kg/m^2 (Table 6.5). In contrast, when using the single referent group the association was attenuated in Asians with a BMI of 18.5-24.9 kg/m^2 suggesting that their baseline hazard was lower compared to normal weight Asians.

E. Discussion

This study examined the complex interplay of acculturation and BMI on type 2 diabetes risk in Asian Americans. Contrary to our expectations, we observed that Asians with lower levels of acculturation and especially those who were born in Asia had a higher risk of diabetes, suggesting Asians might be exposed to risk factors during the different stages of migration.

Environmental[135-137] or behavioral exposures[20] in Asia prior to migration to the US, stress due to resettlement[138] or lower levels of health literacy[139] as well as utilization of preventative services[138] in the US could contribute to the increased diabetes risk in less acculturated Asians.

After controlling for BMI the effect of acculturation on diabetes was further strengthened suggesting that their lower BMI levels might have protected less acculturated Asians from diabetes to some extent. Across levels of BMI, overweight or obesity seemed to further increase the risk of diabetes among Asians with low levels of acculturation. There is a wide array of other potential pathways (e.g. dietary or environmental exposures) through which acculturation can affect diabetes risk, causing Asians with lower levels of acculturation to experience higher diabetes risk. However, we decided to focus on BMI because it is as a strong risk factor for diabetes[125,140], it is the consequence of changes in diet and physical activity due to acculturation[98,99] and it is an easily obtained measure that is collected at routine physician visits and for which successful treatment strategies exist[141].

The diabetes incidence rates observed in our study are comparable to a previous study among Asian Americans using electronic health records[10]. To our knowledge, our study is the first to examine BMI as a potential path through which acculturation can influence diabetes risk among Asian Americans using a principled approach to mediation analysis. Other previous studies used covariate adjustment of the mediator to determine how much of the association of acculturation on diabetes risk can be attributed to BMI. One longitudinal study on the association between acculturation and diabetes in Chinese using data from the Multiethnic Study of Atherosclerosis (MESA) found only 2 cases of diabetes among US-born and 43 cases among foreign-born Asians over a median follow-up time of 5 years[74]. No significant differences were detected (with or without adjustment for BMI), perhaps because of low statistical power.

Another cross-sectional study using data from MESA also did not find an association between an acculturation score (based on place of birth, length of US residence and language spoken at home) and diabetes prevalence with or without adjustment for BMI among 737 Chinese[64]. The Honolulu Heart Program had a larger sample size (n=8,006 Japanese men) but also used a cross-sectional design[58]. As far as we know, this was the only previous study that found an association between acculturation and diabetes. The authors concluded that Japanese who were born in Hawaii had a significantly higher age-adjusted prevalence of diabetes compared to those who were born in Japan (63.6 versus 52.4). This finding remained significant even after adjustment for demographics, BMI, physical activity and diet. However, this study used data from a cohort recruited half a century ago prior to the US obesity epidemic and the rapid changes in the economy, lifestyle and prevalence of overweight and diabetes in Asian countries. Thus, the results from the Honolulu Heart Program may not be applicable to current waves of Asian immigrants to the US and the current US cultural climate.

We used robust methods to assess the mediating effect of BMI on the acculturation-diabetes association. Estimation of direct effects have several assumptions and the validity of our findings is limited by the degree to which these assumptions were met. A key assumption for identification of the controlled direct effect is no unmeasured confounding between: acculturation and diabetes as well as BMI and diabetes[91]. We controlled for age at baseline, education and income as confounders of these associations, however behavioral factors, such as diet, could be considered a source of unmeasured confounding here. Unfortunately, diet was not adequately assessed among Asians in the California Men's Health Study to be evaluated as a confounder. Previous studies showed that a Western dietary pattern, which Asians might adopt after immigrating to the US, was positively associated with type 2 diabetes[142], but was not associated with overweight or obesity[143]. These previous studies suggest that measures of diet might not be associated with both body mass index and diabetes and, thus, diet might not be a major confounder of the BMI-diabetes association. Notably, the potential for diet to lie along the causal pathway between acculturation and BMI precludes identification of acculturation's natural direct and indirect effects, but does not preclude the identification of the controlled effects[76,91,93].

In addition to the confounding assumptions, the soundness of the inferences from these models relies on counterfactual consistency (well defined exposures and mediators). The validity of this assumption with regards to BMI has been questioned[144], since different hypothetical interventions on BMI (e.g. dietary calorie restriction or increased physical activity) could have different independent effects on diabetes incidence. Some authors contend that this issue may limit the causal interpretation of findings such as these[144]. However, this concern is not shared by all[145,146].

Strengths of this study include access to participants' health records for information on repeated, measured weight and height as well as clinical diagnoses of diabetes over a follow-up of 8 years. Additionally, we had a clear temporal sequence of the exposure, the mediator and the outcome.

We combined generational status and length of US residence into a measure of acculturation and exposure to the US environment. We acknowledge that this measure might not fully capture the many dimensions of acculturation. However, the variables used here are highly correlated with more comprehensive acculturation scales[121] and have previously been used in this cohort[134,147]. Length of residence in particular has repeatedly been shown to have high levels of validity and reliability[72,122,123]. Another limitation of this study was that the categories of length of US residence were broad, but sample size did not allow us to use smaller categories.

Participants were members of Kaiser Permanente, had health insurance and were residents of California and, thus, the results are likely not generalizable to all Asian immigrants to the US. Comparing our study population to the 2000 census, we found that our sample had slightly higher levels of education and income compared to the general Asian population in the US[106]; the proportion of individuals with less than a high school degree was 20% in the census compared to 15% in our study according, while the proportion of individuals with an annual household income of <$40,000 was 37% in the census compared to 22% in our study sample. However, the proportion foreign-born in our sample (70%) was comparable to the general Asian population living in California (74%)[148]. Our sample was limited to men and men are more negatively affected by acculturation than women as they are more likely to be in the workforce, which is associated with increased exposure to the host culture[79].

We previously showed that Asian Americans are particularly susceptible to diabetes and have double the risk of diabetes compared to Caucasians[10]. Therefore, it is important to identify diabetes prevention strategies for Asian immigrants to the US. We found that Asians who were less acculturated had an increased risk of diabetes, but generational status and length of US residence are non-modifiable factors that cannot be intervened on to decrease the risk of diabetes among Asian immigrants. However, these indicators can be used to identify individuals at high risk. Using a principled approach to mediation analysis we identified BMI as a modifiable factor that mediates the pathway between acculturation and diabetes. Especially first-generation Asians who have recently immigrated to the US seemed to be protected from diabetes to some extent due to their lower BMI levels. Our finding emphasizes the importance of promoting weight maintenance among recent Asian immigrants who still have low levels of acculturation, while the emphasis might need to be on attainment of a healthy weight among Asian Americans who have already experienced substantial amounts of exposure to the US obesogenic environment. However, future studies on mediating factors other than BMI are needed to fully understand the pathways between acculturation and diabetes risk among Asian Americans.

Table 6.1. Characteristics and crude incidence rates of diabetes (per 1,000 person-years) among Asian men in the California Men's Health Study (2002-2012)

Characteristics	n (%)	Number of cases	Incidence rate (95% CI)
Age at baseline			
44-50 years	945 (17.8)	69	13.94 (10.65, 17.24)
51-55 years	1,308 (24.6)	91	13.05 (10.37, 15.73)
56-60 years	1,053 (19.8)	117	21.08 (17.26, 24.90)
61-65 years	963 (18.1)	107	20.47 (16.59, 24.34)
66-71 years	1,049 (19.7)	112	19.12 (15.58, 22.66)
Body mass index			
<18.5 kg/m^2	45 (0.9)	1	--
18.5-22.9 kg/m^2	1,135 (21.3)	51	7.63 (5.53, 9.72)
23.0-24.9 kg/m^2	1,339 (25.2)	84	12.34 (9.70, 14.98)
25.0-29.9 kg/m^2	2,260 (42.5)	239	20.15 (17.59, 22.70)
≥30.0 kg/m^2	539 (10.1)	121	42.76 (35.14, 50.38)
Education			
≤High school	737 (13.9)	65	16.22 (12.28, 20.16)
Vocational/some college	1,419 (26.7)	152	19.80 (16.65, 22.95)
College graduate	1,772 (33.3)	172	18.11 (15.40, 20.82)
Graduate degree	1,390 (26.1)	107	14.51 (11.76, 17.26)
Annual household income			
<$40,000	1,002 (18.8)	102	18.91 (15.24, 22.58)
$40,000-59,999	1,059 (19.9)	117	20.47 (16.76, 24.18)
$60,000-79,999	937 (17.6)	79	15.59 (12.15, 19.02)
≥$80,000	2,320 (43.6)	198	16.00 (13.77, 18.22)
Acculturation			
1st generation & <10 years	245 (4.6)	19	14.63 (8.05, 21.21)
1st generation & 11-25 years	1,473 (27.7)	150	19.06 (16.01, 22.11)
1st generation & >25 years	1,978 (37.2)	207	19.47 (16.82, 22.12)
2nd generation	623 (11.7)	52	15.44 (11.24, 19.64)
3rd generation	999 (18.8)	68	12.62 (9.62, 15.62)

n = sample size

Table 6.2. Hazard ratios* and 95% confidence intervals of the total effect and the pooled direct effect of acculturation on incident diabetes independent of BMI

	Events	Total effect HR (95 % CI)	Direct effect HR (95% CI)
1st generation & <10 years	19	1.41 (0.85, 2.35)	**1.64 (1.01, 2.65)**
1st generation & 11-25 years	150	**1.56 (1.18, 2.07)**	**1.59 (1.20, 2.11)**
1st generation & >25 years	207	**1.47 (1.13, 1.93)**	**1.46 (1.11, 1.92)**
2nd generation	52	1.22 (0.85, 1.74)	1.15 (0.80, 1.65)
3rd generation	68	REF	REF

*Adjusted for age at baseline, education and income

Table 6.3. Mean BMI (SD) by level of acculturation

Measure of acculturation	BMI (kg/m^2)
1st generation & < 10 years	25.03 (3.36)
1st generation & 11-25 years	24.95 (3.23)
1st generation & >25 years	25.75 (3.55)
2nd generation	26.20 (3.65)
3rd generation	26.51 (3.70)

Table 6.4. Hazard ratios* and 95% confidence intervals of the controlled direct effect between acculturation and incident diabetes within levels of BMI (Wald test for interaction p < 0.0001)

Acculturation	**18.5-24.9 kg/m^2**		**25.0-29.9 kg/m^2**		**≥30.0 kg/m^2**	
	Events	**HR (95% CI)**	**Events**	**HR (95% CI)**	**Events**	**HR (95% CI)**
1st generation & <10 years	5	2.59 (0.94, 7.09)	10	1.28 (0.54, 3.04)	3	**3.67 (1.73, 7.78)**
1st generation & 11-25 years	**48**	**2.65 (1.32, 5.33)**	**73**	**2.11 (1.40, 3.20)**	**29**	1.63 (0.98, 2.73)
1st generation & >25 years	**63**	**2.50 (1.26, 4.95)**	**101**	**1.78 (1.19, 2.64)**	**43**	**1.65 (1.03, 2.63)**
2nd generation	11	1.88 (0.79, 4.44)	22	1.12 (0.66, 1.91)	19	1.16 (0.63, 2.11)
3rd generation	8	REF	33	REF	27	REF

*Adjusted for age at baseline, education and income; Results for BMI <18.5 kg/m^2 not shown since only 1 event was observed in this category.

Table 6.5. Hazard ratios* and 95% confidence intervals of the controlled direct effect between acculturation and incident type 2 diabetes within levels of BMI (Wald test for interaction $p < 0.0001$)

Acculturation	18.5-24.9 kg/m^2		25.0-29.9 kg/m^2		≥30.0 kg/m^2	
	Events	**HR (95% CI)**	**Events**	**HR (95% CI)**	**Events**	**HR (95% CI)**
1st generation & <10 years	5	0.94 (0.40, 2.21)	10	1.28 (0.54, 3.04)	3	**9.74 (4.63, 20.50)**
1st generation & 11-25 years	48	0.96 (0.61, 1.51)	**73**	**2.11 (1.40, 3.20)**	**29**	**4.33 (2.62, 7.16)**
1st generation & >25 years	63	0.91 (0.59, 1.39)	**101**	**1.78 (1.19, 2.64)**	**43**	**4.37 (2.77, 6.89)**
2nd generation	11	0.68 (0.35, 1.34)	22	1.12 (0.66, 1.91)	19	**3.07 (1.70, 5.56)**
3rd generation	8	**0.36 (0.18, 0.75)**	33	REF	27	**2.65 (1.62, 4.35)**

*Adjusted for age at baseline, education and income; Results for BMI <18.5 kg/m^2 not shown since only 1 event was observed in this category.

VII. SYNTHESIS

A. Overview

Although more than 15 million Asians live in the US, Asian Americans are an understudied population in regards to disease risk[2,9,12]. The prevalence of overweight and obesity has increased sharply in Asia[21], but nonetheless the age-adjusted prevalence is still much lower in Asia than in the US (all adults in US: 69%; Asians in US: 41%; Japan: 30%; Philippines: 24%)[22,23]. Asians living in Asia also have a lower age-adjusted diabetes prevalence than Asians living in the US (Asians in the US: 8.2%; Japan: 6.0%; Philippines: 6.6%)[25]. However, after immigration to the US and with increasing time spent in the West, this health advantage seems to diminish and Asian Americans actually have a higher diabetes prevalence than Caucasians (8.2% vs. 6.0%) and double the risk of diabetes than Caucasians[10,27]. The literature on the associations between acculturation and BMI as well as acculturation and diabetes in Asian immigrants is scarce. We aimed to fill the gaps in the literature by determining the associations of exposure to a Western environment on BMI and BMI changes and to determine subsequent diabetes risk in a longitudinal manner. We also used robust methods to determine the mediating effects of BMI on the acculturation-diabetes association to avoid the restrictive assumptions inherent in simple covariate adjustment models. We used data from the California Men's Health Study merged with participants' electronic health records to create a unique dataset to address the research questions posed.

Our research was novel as we were the first to examine BMI patterns in Asians across stages of migration (pre- and post-migration) to confirm the hypothesis that the BMI of Asians increases upon migration to the US. Our study also suggests that the early and middle-adulthood (prior to age 40) might be a vulnerable time period for excess increases in BMI among Asian immigrants. Southeast Asians (Filipinos and Vietnamese) were especially susceptible to excess increases in BMI after immigration to the US. The Philippines and Vietnam have experienced less Westernization than East Asian countries and, thus, Filipino and Vietnamese immigrants are likely more susceptible to exposure to a Western environment upon migration to the US[57,73].

The goal of our second research aim was to expand on these findings and to determine if there is a dose-response relationship between levels of Western exposure and overweight and BMI changes after immigration to the US. As expected, we found that foreign-born, first-generation Asians had a healthier BMI than second- or third-generation, US-born Asians. However, interestingly foreign-born Asians rapidly gained weight during their first 25 years in the US, but they never reached the same level of overweight as their US-born counterparts. We found heterogeneity within the Asian population as the BMI curves differed by Asian subgroup. Filipinos and Koreans were at higher risk of weight gains due to acculturation than Chinese. China has undergone a more rapid rate of Westernization than other Asian countries and, thus, Chinese might have already experienced substantial increases in BMI prior to migration to the US resulting in no additional influence of acculturation on their BMI[57,115].

In our final aim we expanded our conceptual model to include type 2 diabetes as outcome. We expected to find that Asians who were less exposed to a Western environment (e.g. foreign-born and shorter time lived in the US) would have lower risk of diabetes. However, contrary to our expectations, less acculturated Asians actually had a higher risk of diabetes suggesting that environmental[135-137] or behavioral exposures[20] in Asia prior to migration to the US, as well as stress during the difficult process of migration[138] or lower levels of health literacy[139] and utilization of preventative services[138] after immigration to the US can also influence Asian's elevated diabetes risk.

In our previous analyses we established an association between acculturation and BMI as well as an association between acculturation and diabetes. In addition, it is well known that BMI is positively associated with diabetes risk[125,140]. We took these pathways together to determine how much of the effect of acculturation on diabetes risk can be explained by BMI level using robust methods for mediation analysis. The association between acculturation and diabetes was strengthened, when the path through BMI was removed (independent of BMI), especially in first-generation Asians who recently immigrated to the US. Asians who were less acculturated had lower levels of BMI, which might have protected them from diabetes to some extent.

These results provide novel insights into the influence of exposure to a Western environment on BMI and diabetes risk among Asian immigrants. Asians are particularly susceptible to elevated cardiovascular disease risk than other ethnic groups due to their higher percentage of body fat and abdominal obesity[7]. Thus, even small increases in BMI after immigration and assimilation to a Western environment might exacerbate the cardiovascular disease burden in Asian American. This research emphasizes the importance of prevention efforts are in this vulnerable ethnic group. Measures of acculturation, such as generational status or length of US residence, can be used to identify these individuals at risk for excess BMI increases and who might benefit from counseling or interventions focused on maintaining a healthy weight or diabetes prevention and treatment.

B. Strengths

In this dissertation we posed novel questions, made new linkages in data sources, addressed important gaps in the literature and made substantial contributions to inform policy. The methodologies used were state of the art and we were the first to: (1) determine the difference in BMI over time by place of residence in Asians living in Asia and Asians Americans; (2) determine indicators of acculturation as determinants of BMI change in Asian Americans; (3) determine the role of BMI as a mediator of risk of diabetes in Asian Americans as a result of exposure to a Western environment; and (4) link extant data on Chinese, Japanese, Korean, Filipino and Vietnamese men from the California Men's Health Study with Kaiser Permanente Electronic Health Records.

Other strengths of this dissertation included the large sample size of Asian Americans, an understudied population. California houses the largest proportion of Asian Americans (~4.2 million) and, thus, data from California include larger representative samples of Asian Americans than national surveys. Asian subgroups were examined separately to determine heterogeneity by country/region of origin in the association between acculturation and BMI change. Additionally, we had access to repeated, clinically measured weight and height as well as diabetes diagnoses over a follow-up of 8 years.

C. Limitations

Unfortunately we were not able to determine the underlying factors that might have contributed to the differential changes in BMI by place of residence or level of acculturation. Immigration and acculturation likely lead to changes in lifestyle (e.g. changes in diet or physical activity), which subsequently can influence BMI. In Aim 1 we used recalled weight at ages 30, 40, 50 and 60, but we found that the correlation coefficients between clinically measured weight at age 50 (n=91) and at age 60 (n=318) from participants' Kaiser Permanente electronic health records compared to recalled weight at these ages at baseline were 0.95 and 0.93, respectively.

We used generational status, length of US residence and age at immigration as indicators of exposure to a Western obesogenic environment. These factors are commonly used proxies, but might not fully capture the multidimensional influences of acculturation. Unfortunately indicators that measure the degree to which an individual is acculturated (e.g. language spoken at home, cultural identity, stress levels, social networks) were not assessed in the California Men's Health Study. Since acculturation is such a complex phenomenon that cannot be captured in a simple quantitative measure, our goal was to use valid and reliable indicators that measure exposure to the US environment. The proxies of acculturation used here are highly correlated with more comprehensive acculturation scales[121]. Length of residence has repeatedly been shown to have high levels of validity and reliability[72,122,123]. The categories of length of US residence and age at immigration we used were broad. Unfortunately, sample size limitations did not allow us to use smaller categories.

The Asians included in this dissertation might not be generalizable to all Asian immigrants to the US since they were members of Kaiser Permanente and had health insurance. Compared to the general Asian population living in the US, our study population had slightly higher levels of education (20% vs. 15% with less than a high school degree) and income (37% vs. 22% with annual household income of <$40,000)[106]. However, the proportion foreign-born in our study population was comparable to the general Asian population living in California (70% vs. 74%)[148].

Immigrants to the US are also a self-selected group and reasons for migration might have differed by Asian subgroups. In addition, our research was limited to Asian men. Men tend to be more negatively affected by acculturation than women as they are more likely to be in the workforce, which is associated with increased exposure to the host culture[79].

Although we used state of the art, robust methods to answer these research questions, all models have specific assumptions and the validity of our findings is limited by the degree to which these assumptions were met. Nevertheless, this study provided the unique opportunity to examine the complex interplay of immigration, acculturation, BMI and diabetes among Asians.

D. Future directions

Our findings are limited to Asian men and, thus, future studies are needed to confirm our findings in Asian women. In addition, the role of other potential intermediates in the pathway between acculturation and diabetes need to be examined (e.g. diet and physical activity). Immigration and acculturation likely result in lifestyle changes that can influence diabetes risk through changes in BMI, but also independent of BMI (e.g. physical activity increases translocation of GLUT4 receptor). Other studies have demonstrated that after immigration to the US, Chinese, Japanese and Koreans increase their intake of cholesterol, saturated fat, sweets, dairy and fruit, but decrease their consumption of traditional foods, meat and meat alternatives and vegetables [98,116,117]. With increasing time spent in a Western country, portion sizes, frequency of dining out and consumption of convenience foods increases among Chinese[118]. Physical activity tends to decrease upon immigration to a Western country[99], but increases as Asian immigrants have lived longer in the US and become more acculturated[35,119,120]. However, to our knowledge so far no study examined if these changes in diet and physical activity can explain the association between acculturation and diabetes risk and if so, if diet and physical activity can explain parts of the effect that are not captured by BMI. Such studies will provide further insight into the specific risk factors that need to be targeted by diabetes prevention efforts in Asian immigrants.

Finally, this dissertation research emphasizes the importance of more research on diabetes risk factors in foreign-born Asians who have a higher risk of diabetes than their US-born counterparts. Future studies need to examine potential diabetes risk factors at the different stages of migration (e.g. environmental[135-137] or behavioral risk factors[20] in Asia, migration stress[138], low health literacy after immigration to the US[139]).

APPENDIX: BASELINE CHARACTERISTICS BY AGE AT IMMIGRATION

We also examined the baseline characteristics for the analysis in Chapter 4 by age at immigration to determine if Asians who immigrated earlier in life might differ in demographics or socioeconomic factors from Asian who immigrated later in life. The baseline characteristics are presented for all Asians combined as well as by Asian subgroup.

Table A.1. Characteristics of study sample by age at immigration among all Asians combined and by Asian subgroup, California Men's Health Survey (2002-03)[a]

Characteristics	Immigration between ages 19 & 30	Immigration between ages 30 & 40	Immigration between ages 40 & 50	Immigration between ages 50 & 60	Immigration after age 60
All Asians (n=977)					
n [%]	53.3	16.1	19.9	8.6	2.1
Age at baseline in years [mean SD[b])]	50.7 (3.1)	51.0 (3.8)	58.0 (5.3)	65.2 (3.5)	67.9 (2.5)
Education [%]					
≤ High school	17.1	25.5	17.0	23.8	23.8
Vocational/some college	28.8	20.4	29.9	25.0	33.3
College graduate	31.7	33.1	39.2	41.7	23.8
Graduate degree	22.5	21.0	13.9	9.5	19.1
Annual household income [%]					
<$40,000	13.4	22.9	32.0	60.7	76.2
$40,000-59,999	22.1	28.7	22.7	17.9	19.1
$60,000-79,999	20.7	13.4	18.6	15.5	0
≥$80,000	43.8	35.0	26.8	6.0	4.8
Chinese (n=480)					
n [%]	49.0	18.8	19.8	10.0	2.5
Age at baseline in years [mean (SD[2])]	50.4 (3.0)	50.1 (3.4)	57.4 (5.5)	66.2 (3.0)	67.7 (2.4)
Education [%]					
≤ High school	21.7	33.3	22.1	20.8	16.7
Vocational/some college	23.8	18.9	31.6	29.2	41.7
College graduate	19.6	17.8	30.5	41.7	25.0
Graduate degree	34.9	30.0	15.8	8.3	16.7
Annual household income [%]					
<$40,000	10.2	21.1	26.3	66.7	75.0
$40,000-59,999	19.2	24.4	26.3	16.7	25.0
$60,000-79,999	17.5	14.4	16.8	14.6	0
≥$80,000	53.2	40.0	30.5	2.1	0

Characteristics	Immigration between ages 19 & 30	Immigration between ages 30 & 40	Immigration between ages 40 & 50	Immigration between ages 50 & 60	Immigration after age 60
Southeast Asians (n=453)					
n [%]	56.5	13.7	20.5	7.3	2.0
Age at baseline in years [mean (SD[2])]	50.9 (3.1)	51.9 (4.1)	48.5 (5.1)	63.4 (3.6)	68.2 (2.8)
Education [%]					
≤ High school	12.1	14.5	11.8	27.3	33.3
Vocational/some college	34.4	24.2	30.1	21.2	22.2
College graduate	43.0	53.2	47.3	42.4	22.2
Graduate degree	10.6	8.1	10.8	9.1	22.2
Annual household income [%]					
<$40,000	16.8	25.8	36.6	54.6	77.8
$40,000-59,999	24.2	32.3	19.4	18.2	11.1
$60,000-79,999	21.9	12.9	21.5	18.2	0
≥$80,000	37.1	29.0	22.6	9.1	11.1

[a] Includes only participants for whom age at immigration could be attributed to the specific age intervals; the sample of other East Asians was too small (n=44) to analyze by age at immigration

[b] SD = standard deviation

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